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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Bob) Shiao Examiner #: 7951 Date: 05/1[illegible]
Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/750,87[illegible]
Location (Bldg/Room#): RCM (Mailbox #): 5A07 Results Format Preferred (circle): PAPER
5C18

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the followin

Title of Invention: indole-3-yl derivs

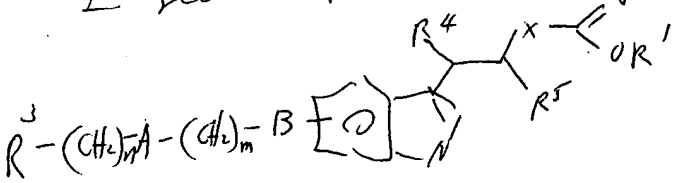
Inventors (please provide full names): Winkler et al

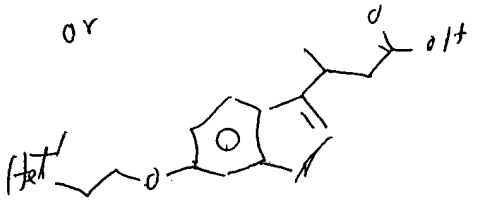
Earliest Priority Date: _____

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of t Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

***For Sequence Searches Only** Please include all pertinent information (parent, child, divisional, or issued patent numbers) al appropriate serial number.*

I Such cpd I. or Ij. (see claim 1, 17, 20)





* R, R', R², R⁴, R⁵, R⁶ Sub. ie. R or hetaryl
* n, m is 0
* A, B is O, S, CONH, NHC bond
* X is alkylene

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Date Searcher Picked Up: _____
Date Completed: _____
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Type of Search

_____ NA Sequence (#)
_____ AA Sequence (#)
_____ Structure (#)
_____ Bibliographic
_____ Litigation
_____ Fulltext
_____ Other

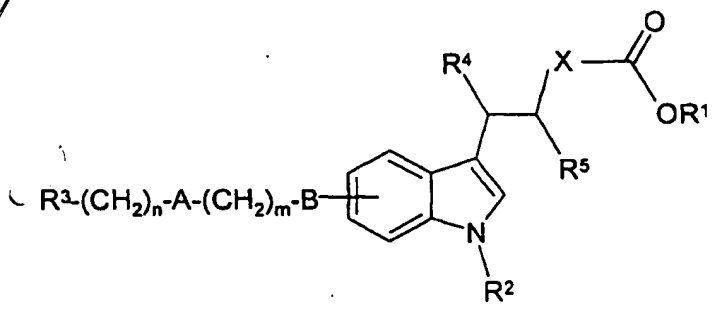
Vendors and cost where applicabl

_____ STN _____ Dial
_____ Questel/Orbit _____ Le
_____ Westlaw _____ WW
____ In-house sequence systems
___ Commercial ___ Oligomer ___
___ Interference ___ SPDI ___
_____ Other (specify)

Patent Claims

We Claim:

1. A compound of the formula I



I

in which

A and B are each, independently of one another, O, S, NH, NR^7, CO, CONH, NHCO or a direct bond,

X is alkylene having 1 to 2 carbon atoms which is unsubstituted or monosubstituted by R^4 or R^5, or a direct bond,

R^1 is H, Z or $-(CH_2)_o$-Ar,

R^2 is H, R^7 or -C(O)Z,

R^3 is NHR^6, $-NR^6-C(=NR^6)-NHR^6$, $-C(=NR^6)-NHR^6$, $-NR^6-C(=NR^9)-NHR^6$, Het[1] or $-C(=NR^9)-NHR^6$,

R^4 and R^5 are each, independently of one another, H, oxo, R^7, $-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o$-Ar, $-C(O)-(CH_2)_o-R^7$, $-C(O)-(CH_2)_o$-Het, Het, NHR^6, NHAr, NH-Het, $CONH-R^7$, $CONH-(CH_2)_o$-Ar, $CONH-(CH_2)_o$-Het, OR^7, OAr, OR^6 or O-Het,

R^6 is H, $-C(O)R^7$, -C(O)-Ar, -C(O)-Het, R^7, $COOR^7$, $COO-(CH_2)_o$-Ar, $COO-(CH_2)_o$-Het, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, $-(CH_2)_o$-Ar, $COOR^1$, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, $N(R^1)_2$, $NH-C(O)R^1$, $NHCOOR^1$, COOH, COOZ or $C(O)R^1$,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het is a saturated, partially or fully unsaturated monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members, where 1 or 2 N and/or 1 or 2 S or O atoms may be present and the heterocyclic radical may be monosubstituted or disubstituted by R^8,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

n is 0, 1 or 2,

m is 0, 1, 2, 3, 4, 5 or 6, and

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

2. An enantiomer of a compound according to Claim 1.

3. A compound according to Claim 1, wherein X is a direct bond.

4. A compound according to Claim 1, wherein

B is O,

R^4 is R^7, $(CH_2)_o$-Ar or Het,

o is 0 or 1,

R^5 is H, and

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms.

5. A compound according to Claim 1, selected from,

a) 3-phenyl-3-{6-[3-(pyridin-2-ylamino)propoxy]-1H-indol-3-yl} propionic acid;

b) 3-phenyl-3-[6-(pyridin-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

c) 3-phenyl-3-[6-(benzimidazol-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

d) 3-phenyl-3-[6-(imidazol-2-ylamidocarboxymethoxy)indol-3-yl] propionic acid;

e) 3-{6-[3-(4,5-dihydro-1H-imidazol-2-ylamino)propoxy]-1H-indol-3-yl}-3-phenylpropionic acid;

f) 3-phenyl -3-[6-[3-(guanidinopropoxy]indol-3-yl}propionic acid;

g) 3-(benzo[1,2,5]thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid;

and physiologically acceptable salts and solvates thereof.

6. A process for the preparation of a compound according to Claim 1 and its salts and solvates, wherein

a) a compound of the formula I is liberated from one of its functional derivatives by treatment with a solvolyzing or hydrogenolyzing agent,

or

b) a radical R^1, R^2, R^3, R^4, R^5 and/or R^6 is converted into another radical R^1, R^2, R^3, R^4, R^5 and/or R^6,

by

i) converting an amino group into a guanidino group by reaction with an amidating agent,

ii) saponifying an ester,

iii) alkylating or acylating an amino group,

iv) converting a cyano group into an amidino group,

and/or a base or acid of the formula I is converted into one of its salts.

7. A therapeutic active ingredient comprising a compound according to Claim 1 and physiologically acceptable salts or solvates thereof.

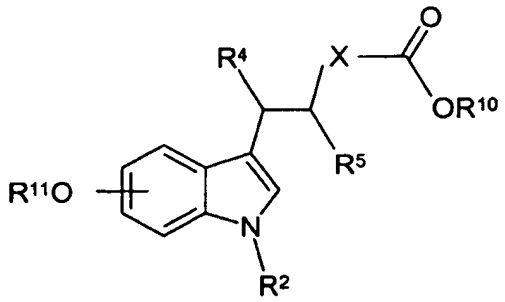
8. An integrin inhibitor comprising a compound according to Claim 1 and physiologically acceptable salts or solvates thereof.

9. A pharmaceutical preparation, comprising at least one compound according to Claim 1 and/or physiologically acceptable salts or solvates thereof.

10. A process for the preparation of a medicament comprising admixing a compound of according to Claim 1 and/or physiologically acceptable salts or solvates thereof with at least one solid, liquid, or semi-liquid excipient or auxiliary or optionally, one or more other active ingredient.

11. A method of treating thromboses, cardiac infarction, coronary heart diseases, arteriosclerosis, inflammations, rheumatic arthritis, macular degenerative disease, diabetic retinopathy, a tumour by inhibition of metastasis, a tumour by initiation of apoptosis, tumour induced angiogenesis disease, osteoporosis, and/or infections and restenosis after angioplasty comprising administering to a patient in need thereof a compound according to Claim 1 and/or physiologically acceptable salts or solvates thereof.

12. Compounds of the formula IIa



IIa

in which R^2, R^4 and R^5 are as defined in Claim 1,

R^1 is H, Z or $-(CH_2)_o$-Ar,

R^2 is H, R^7 or -C(O)Z,

R^6 is H, -C(O)R^7, -C(O)-Ar, -C(O)-Het, R^7, COOR^7, COO-$(CH_2)_o$-Ar, COO-$(CH_2)_o$-Het, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, -$(CH_2)_o$-Ar, COOR^1, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, N$(R^1)_2$, NH-C(O)R^1, NHCOOR^1, COOH, COOZ or C(O)R^1,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

n is 0, 1 or 2,

m is 0, 1, 2, 3, 4, 5 or 6, and

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

14. A compound according to Claim 1, wherein

X is a bond,

B is O,

R^1 is H,

R^4 is Het,

A is a bond,

and

R^3 is Het^1.

15. A compound according to claim 14, wherein Het^1 is pyridine which may be substituted by NHZ where Z is alkyl having 1 to 6 carbon atoms.

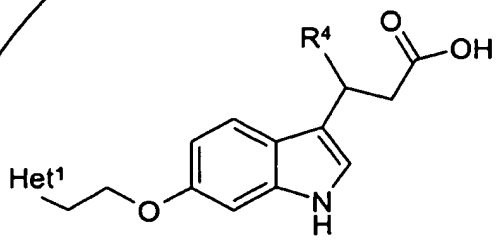
16. A compound according to claim 14, wherein R^4 is benzothiadiazol .

17. A compound according to claim 1, which is 3-(benzo[1,2,5]thiadiazol-5-yl)-3-{6-[2-(6-methylamino-pyridin-2-yl)-ethyloxy]-indol-3-yl}-propionic acid.

18. A compound according to claim 1, in racemic form.

19. A compound according to claim 1, in the form of substantially only one of its enantiomers.

20. A compound of the formula Ij



Ij

in which

R^3 is NHR^6, $-NR^6-C(=NR^6)-NHR^6$, $-C(=NR^6)-NHR^6$, $-NR^6-C(=NR^9)-NHR^6$, Het^1or $-C(=NR^9)-NHR^6$,

R^4 is H, oxo, R^7, $-(CH_2)_o-Ar$, $-C(O)-(CH_2)_o-Ar$, $-C(O)-(CH_2)_o-R^7$, $-C(O)-(CH_2)_o-Het$, Het, NHR^6, NHAr, NH-Het, $CONH-R^7$, $CONH-(CH_2)_o-Ar$, $CONH-(CH_2)_o-Het$, OR^7, OAr, OR^6 or O-Het,

R^6 is H, $-C(O)R^7$, -C(O)-Ar, -C(O)-Het, R^7, $COOR^7$, $COO-(CH_2)_o-Ar$, $COO-(CH_2)_o-Het$, SO_2-Ar, SO_2R^7 or SO_2-Het,

R^7 is alkyl having 1 to 10 carbon atoms or cycloalkyl having 3 to 10 carbon atoms,

R^8 is Hal, NO_2, CN, Z, $-(CH_2)_o-Ar$, $COOR^1$, OR^1, CF_3, OCF_3, SO_2R^1, NHR^1, $N(R^1)_2$, $NH-C(O)R^1$, $NHCOOR^1$, COOH, COOZ or $C(O)R^1$,

R^9 is CN or NO_2,

Z is alkyl having 1 to 6 carbon atoms,

Ar is aryl which is unsubstituted or monosubstituted or polysubstituted by R^8,

Hal is F, Cl, Br or I,

Het is a saturated, partially or fully unsaturated monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members, where 1 or 2 N and/or 1 or 2 S or O atoms may be present and the heterocyclic radical may be monosubstituted or disubstituted by R^8,

Het^1 is a monocyclic or bicyclic heterocyclic radical having 5 to 10 ring members and 1 to 4 N atoms each of which may be unsubstituted or monosubstituted or disubstituted by Hal, R^7, OR^7, CN, NHZ, oxo or NO_2,

o is 0, 1 or 2,

and physiologically acceptable salts and solvates thereof.

21. A pharmaceutical composition comprising a compound of claim 17 and a pharmaceutically acceptable carrier.

22. A method of treating thromboses, cardiac infarction, coronary heart diseases, arteriosclerosis, inflammations, rheumatic arthritis, macular degenerative disease, diabetic retinopathy, a tumour by inhibition of metastasis, a tumour by initiation of apoptosis, tumour induced angiogenesis disease, osteoporosis, and/or infections and restenosis after angioplasty comprising administering to a patient in need thereof a compound according to Claim 17 and/or physiologically acceptable salts or solvates thereof.

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Bib Data Sheet

CONFIRMATION NO. 3230

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/750,879	01/05/2004 RULE	514	1626	MERCK-2481-P1

APPLICANTS

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Simon Goodman, Griesheim, GERMANY;
Rudolf Gottschlich, Mainz, GERMANY;

** CONTINUING DATA **********

This application is a CIP of 10/203,406 08/09/2002 PAT 6,743,810
which is a 371 of PCT/EP01/00084 01/05/2001

** FOREIGN APPLICATIONS **********

GERMANY 10006139.7 02/11/2000 filed on 10/203,406

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 04/08/2004

Foreign Priority claimed	STATE OR	SHEETS	TOTAL	INDEPENDENT
☒ yes ☐ no				
35 USC 119 (a-d) conditions met ☐ yes ☐ no ☐ Met after Allowance				
Verified and Acknowledged Examiner's Signature Initials	COUNTRY GERMANY	DRAWING 0	CLAIMS 22	CLAIMS 3

ADDRESS
23599
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SUITE 1400
ARLINGTON , VA
22201

TITLE
Indol-3-yl derivatives

FILING FEE	FEES: Authority has been given in Paper	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of

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L6              STR L1
L7            9 S L6 SSS SAM SUB=L5
L8          140 S L6 SSS FUL SUB=L5
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L10          45 S L8
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L3              STR
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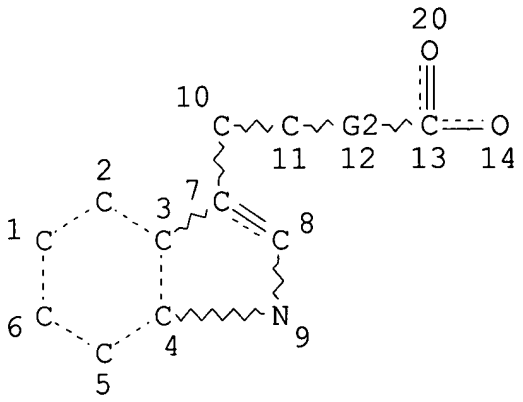

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
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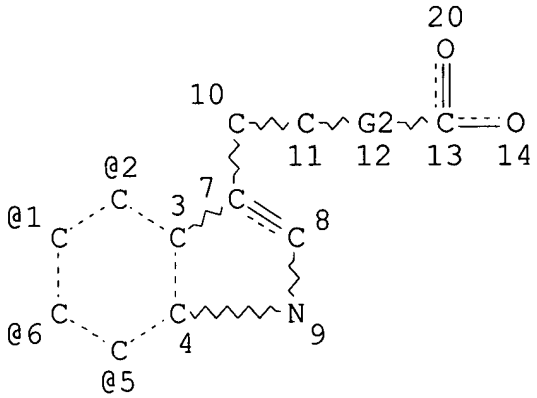

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REP G3=(0-8) A
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STEREO ATTRIBUTES: NONE
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=> d l11 1-35 ibib abs hitstr hitrn

L11 ANSWER 1 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:316692 ZCA
TITLE: Preparation of indolylcarboxamide derivatives as inhibitors of p38 kinase
INVENTOR(S): Mavunkel, Babu J.; Chakravarty, Sarvajit; Perumattam, John J.; Dugar, Sundeep; Lu, Qing; Liang, Xi
PATENT ASSIGNEE(S): Scios, Inc., USA
SOURCE: U.S., 65 pp., Cont.-in-part of U.S. 6,589,954.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6867209	B1	20050315	US 2000-575060	200005 19
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US 6130235	A	20001010	US 1998-128137	199808 03
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US 6340685	B1	20020122	US 1999-275176	199903 24
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US 6589954	B1	20030708	US 1999-316761	199905 21
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US 2003158417	A1	20030821	US 2002-146703	200205 14
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US 2003144520	A1	20030731	US 2002-157048	200205 28
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US 6864260	B2	20050308		
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US 2003195355	A1	20031016	US 2002-156997	200205 28
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PRIORITY APPLN. INFO.:			US 1998-86531P	P 199805 22
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			US 1998-128137	A2 199808 03
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			US 1999-275176	A2 199903 24
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			US 1999-316761	A2 199905 21

<-- US 1999-154594P P 19990917
<-- US 2000-202608P P 20000509
<-- US 2000-575060 A1 20000519
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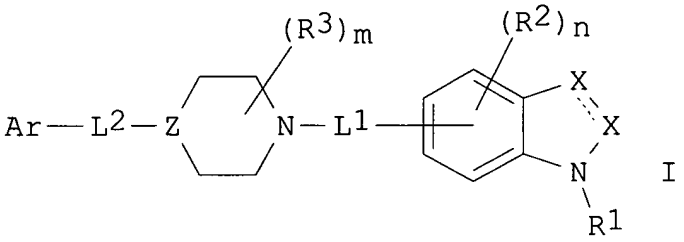
OTHER SOURCE(S): MARPAT 142:316692

GI



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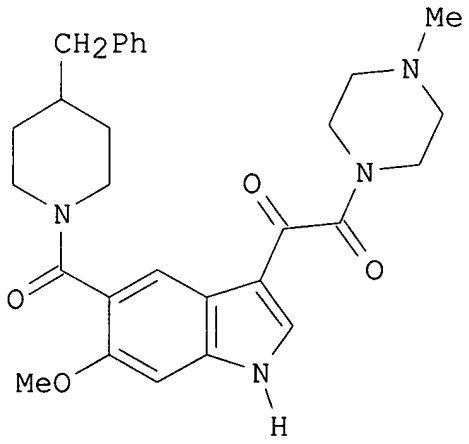


II

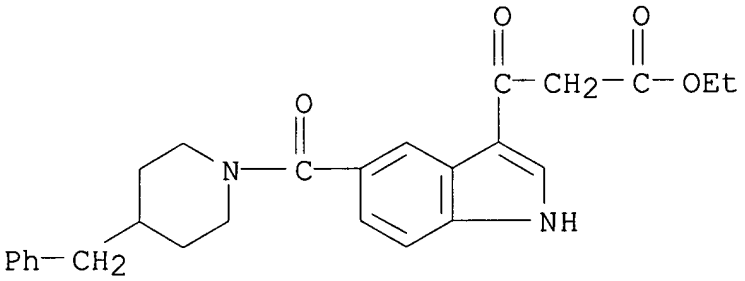
AB Title compds. I [X independently = CA, CR4A, CR5, CR52, NR6, or N; L1 = CO, SO2, or alkylene; L2 = (un)substituted-alkylene or

-alkenylene; Ar = (un)substituted aryl group with substituents consisting of alkyl, alkenyl, halo, CN, etc.; Z = N or CR7 wherein R7 = H or non-interfering substituent; R1 = H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, etc.; R2 independently = halo, alkyl, OH, alkoxy, etc.; R3 independently = CN, CF3, NO2, alkyl, aryl, acyl, etc.; R4 = H, halo, alkyl or alkenyl; R5 independently = H, halo, alkyl, OH, etc.; R6 = H, alkyl, alkenyl, aryl, acyl, aroyl, etc.; A = -WiCOXjY wherein Y is COR8 wherein R8 = H, (un)substituted-alkyl, -alkenyl, -alkynyl, etc.; W and X = (un)substituted-alkylene, -alkenylene, -alkynylene; Y = tetrazole, 1,2,3-triazole, 1,2,4-triazole, or imidazole and each of i and j independently = 0 or 1; m = 0-4; n = 0-3], and their pharmaceutically acceptable salts are prepd. and disclosed as useful for treatment of rheumatoid arthritis. Thus, e.g., II, was prepd. by carbonylation of 6-methoxy-(4-benzylpiperidinyl)-indole-5-carboxamide with oxalyl chloride and subsequent amination using 4-methylpiperazine. ELISA assays for evaluation of inhibition of p38 kinase by I revealed that all compds. of the invention possessed IC50 values in the range of 0.1-1.5 .mu.M. I as inhibitors of p38 kinase should prove useful in the treatment of rheumatoid arthritis.

IT **309915-11-5P**
(prepn. of indolylcarboxamide derivs. as p38 kinase inhibitors)

RN 309915-11-5 ZCA

CN 1H-Indole-3-propanoic acid, .beta.-oxo-5-[[4-(phenylmethyl)-1-piperidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **309915-11-5P**
(prepn. of indolylcarboxamide derivs. as p38 kinase inhibitors)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 141:123559 ZCA

TITLE: A preparation of indole derivatives, useful as integrin inhibitors

INVENTOR(S): Wiesner, Matthias; Goodman, Simon; Gottschlich, Rudolf

PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 203,406.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138284	A1	20040715	US 2004-750879	20040105
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DE 10006139	A1	20010816	DE 2000-10006139	20000211
WO 2001058893	A2	20010816	WO 2001-EP84	20010105
			<--	
WO 2001058893	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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US 2002-203406	A2	

200208
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OTHER SOURCE(S): MARPAT 141:123559
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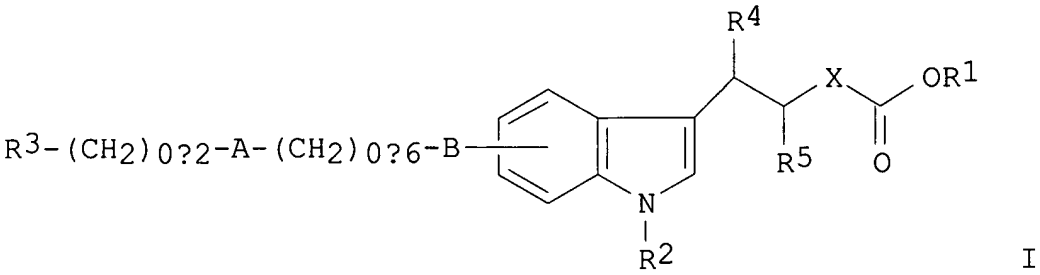


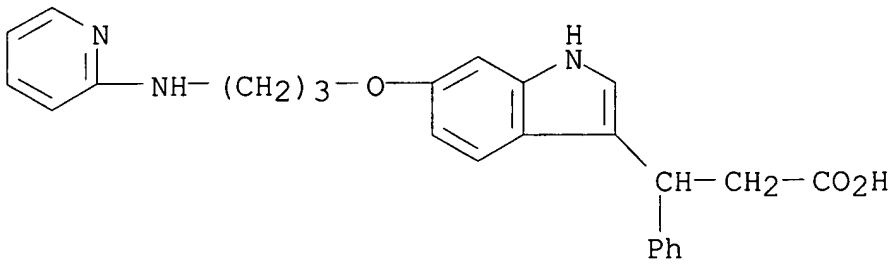
I

AB The invention relates to a prepn. of indole derivs. of formula I [wherein: A and B are independently selected from O, S, NH, NH, C(O), or C(O)NH, etc.; X is (un)substituted alkylene; R1 is H, C1-6alkyl, or (CH2)0-2-aryl; R2 is H, (cyclo)alkyl, or -C(O)-alkyl; R3 is NH2, -NHC(O)-alkyl, -NH(CO)-aryl, etc.; R4 and R5 are independently selected from H, oxo, (cyclo)alkyl, C(O)NH2, or NH-heterocycle, etc.], useful as integrin inhibitors (no biol. data). Compds. of formula I can be employed for combating thromboses, cardiac infarction, coronary heart diseases, arteriosclerosis, inflammations, tumors, osteoporosis, rheumatic arthritis, macular degenerative disease, and diabetic retinopathy, etc. The invention compds. act as integrin inhibitors, inhibiting, in particular, the interaction of the .alpha.v-, .beta.3- and .beta.5-integrin receptors with ligands (no biol. data).

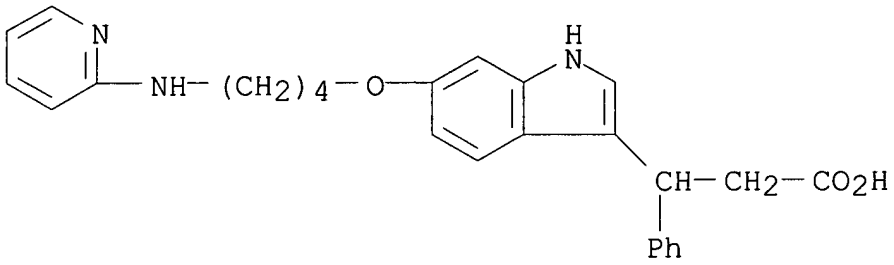
IT **354822-33-6P 354822-34-7P 354822-37-0P**
354822-38-1P 354822-39-2P 354822-40-5P
354822-49-4P 354822-62-1P 354822-69-8P
354822-70-1P 354822-76-7P 354822-83-6P
354822-85-8P 354822-86-9P 354822-88-1P
354822-89-2P 354822-90-5P 354822-93-8P
354822-95-0P 354822-97-2P 354823-01-1P
354823-03-3P 354823-06-6P 354823-11-3P
354823-18-0P 354823-25-9P 354823-28-2P
354823-43-1P 354823-47-5P 354823-49-7P
354823-52-2P 354823-55-5P 724478-49-3P
724478-50-6P 724478-55-1P 724478-56-2P
724478-60-8P
(prepn. of indole derivs., useful as integrin inhibitors)

RN 354822-33-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-

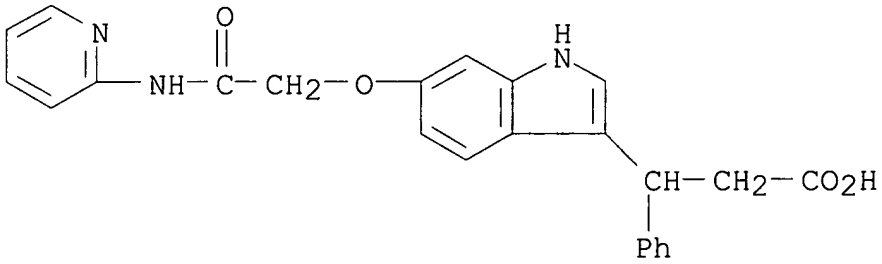
pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



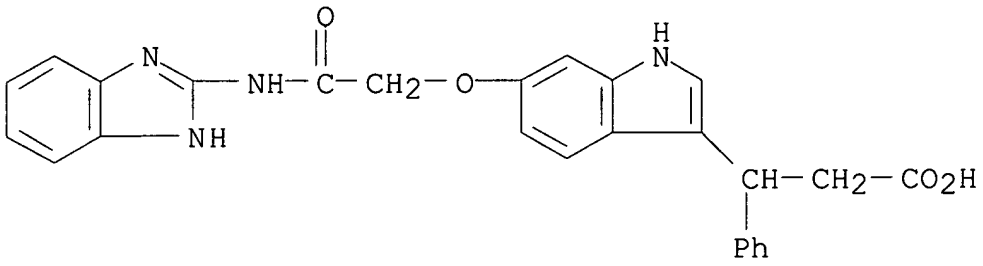
RN 354822-34-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-(2-pyridinylamino)butoxy]- (9CI) (CA INDEX NAME)



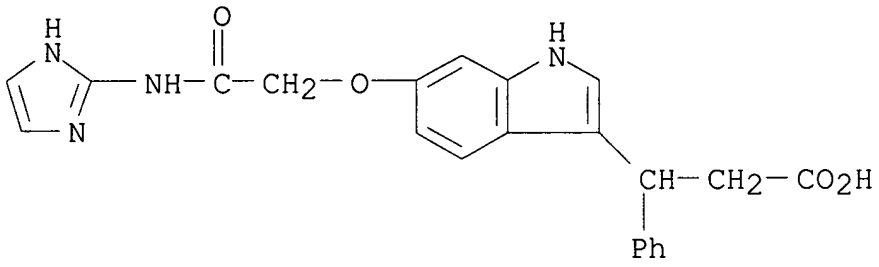
RN 354822-37-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-oxo-2-(2-pyridinylamino)ethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



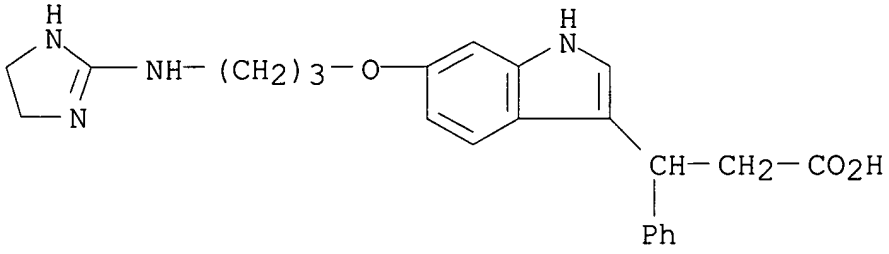
RN 354822-38-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-benzimidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



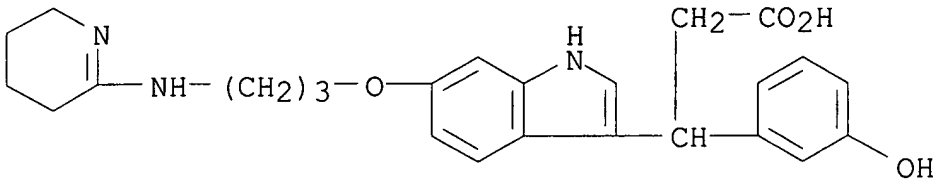
RN 354822-39-2 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-imidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



RN 354822-40-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



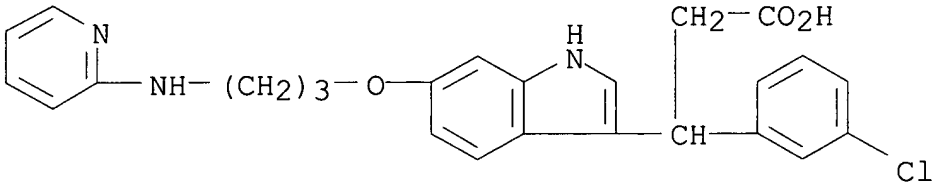
RN 354822-49-4 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3-hydroxyphenyl)-6-[3-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]propoxy]- (9CI) (CA INDEX NAME)



RN 354822-62-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3-chlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

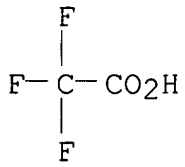
CM 1

CRN 354822-46-1
CMF C25 H24 Cl N3 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

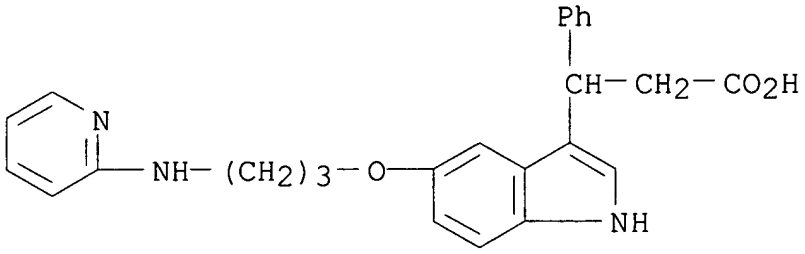


RN 354822-69-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

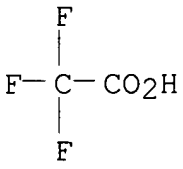
CRN 354822-36-9

CMF C25 H25 N3 O3



CM 2

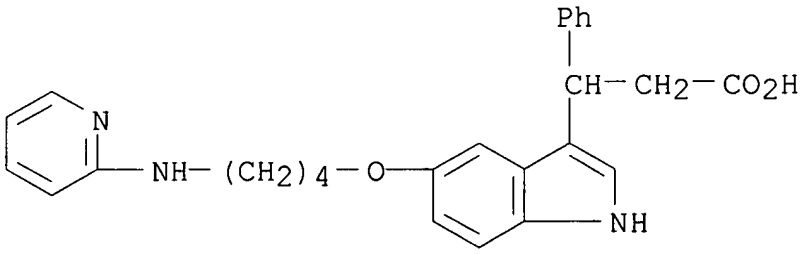
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-70-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[4-(2-pyridinylamino)butoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

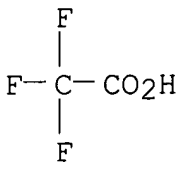
CM 1

CRN 354822-35-8
CMF C26 H27 N3 O3



CM 2

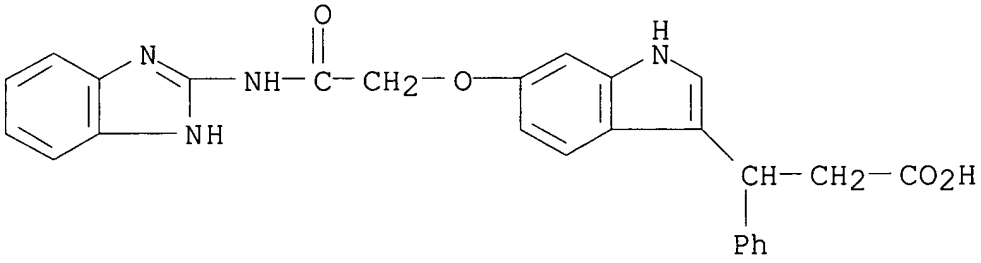
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-76-7 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-benzimidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

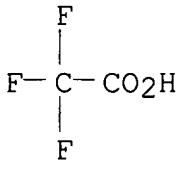
CM 1

CRN 354822-38-1
CMF C26 H22 N4 O4



CM 2

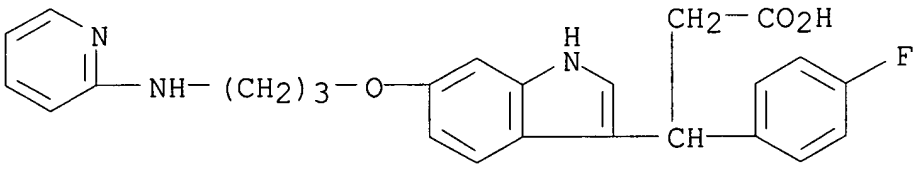
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-83-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(4-fluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

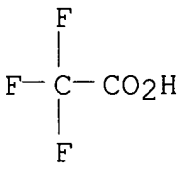
CM 1

CRN 354822-41-6
CMF C25 H24 F N3 O3



CM 2

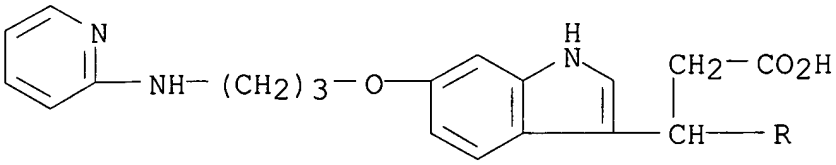
CRN 76-05-1
CMF C2 H F3 O2

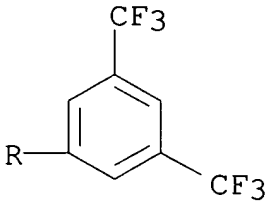


RN 354822-85-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[3,5-bis(trifluoromethyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

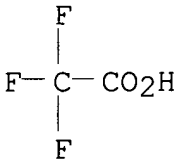
CRN 354822-84-7
CMF C27 H23 F6 N3 O3





CM 2

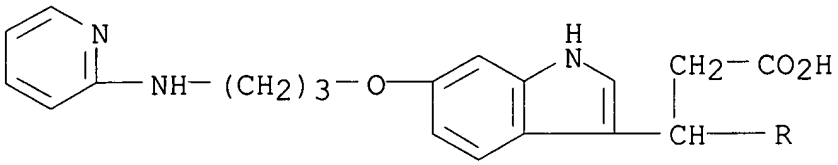
CRN 76-05-1
CMF C2 H F3 O2

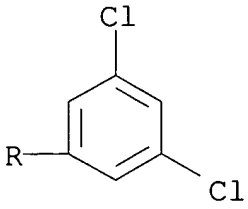


RN 354822-86-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3,5-dichlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

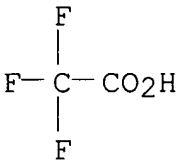
CRN 354822-42-7
CMF C25 H23 Cl2 N3 O3





CM 2

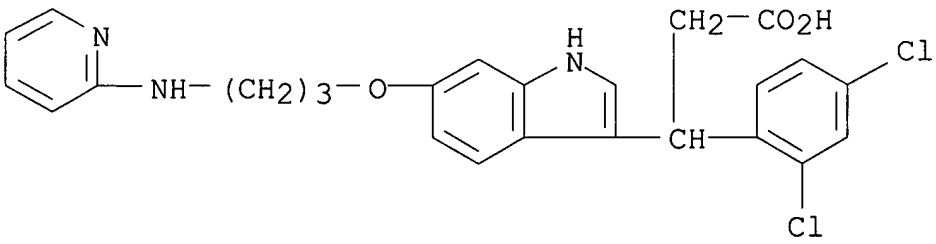
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-88-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2,4-dichlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

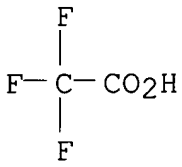
CM 1

CRN 354822-87-0
CMF C25 H23 Cl2 N3 O3



CM 2

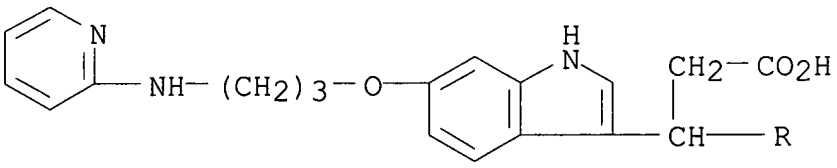
CRN 76-05-1
CMF C2 H F3 O2

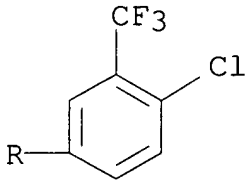


RN 354822-89-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[4-chloro-3-(trifluoromethyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

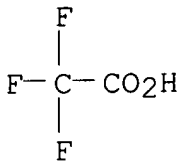
CRN 354822-43-8
CMF C26 H23 Cl F3 N3 O3





CM 2

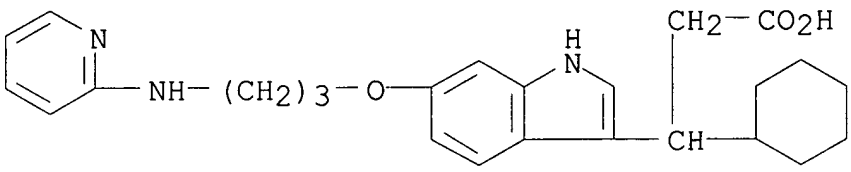
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-90-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-cyclohexyl-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

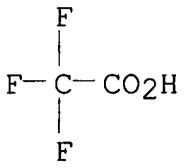
CM 1

CRN 354822-44-9
CMF C25 H31 N3 O3



CM 2

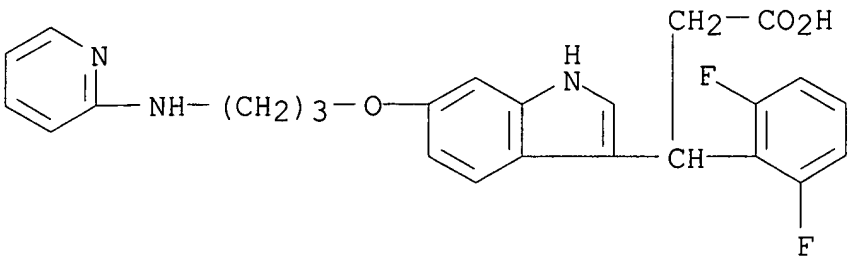
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-93-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2,6-difluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

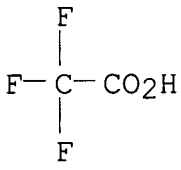
CM 1

CRN 354822-92-7
CMF C25 H23 F2 N3 O3



CM 2

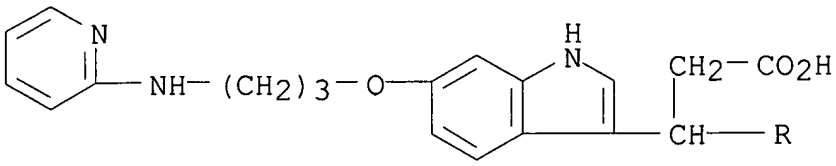
CRN 76-05-1
CMF C2 H F3 O2

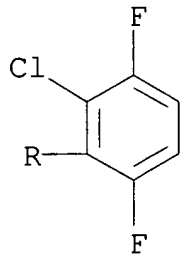


RN 354822-95-0 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2-chloro-3,6-difluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

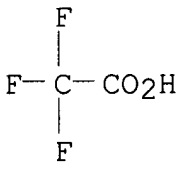
CRN 354822-94-9
CMF C25 H22 Cl F2 N3 O3





CM 2

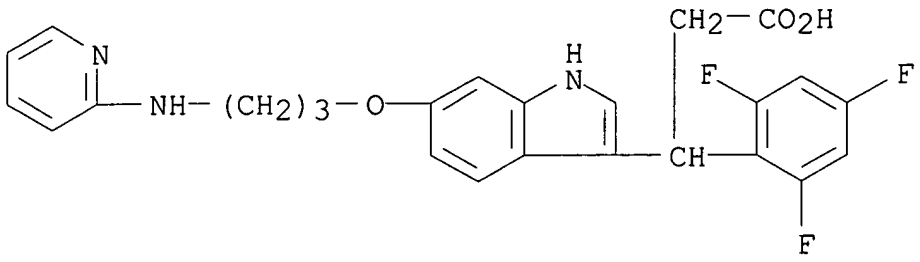
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-97-2 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-(2,4,6-trifluorophenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

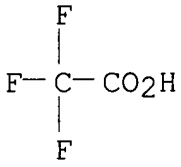
CM 1

CRN 354822-96-1
CMF C25 H22 F3 N3 O3



CM 2

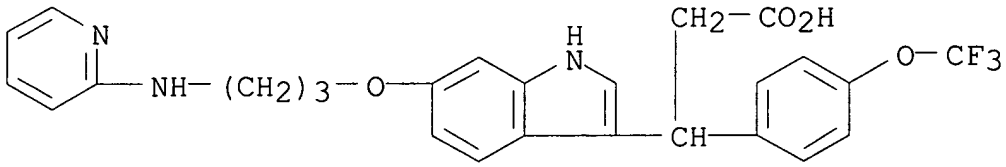
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-01-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-[4-(trifluoromethoxy)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

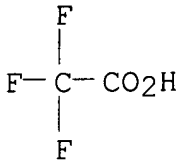
CM 1

CRN 354823-00-0
CMF C26 H24 F3 N3 O4



CM 2

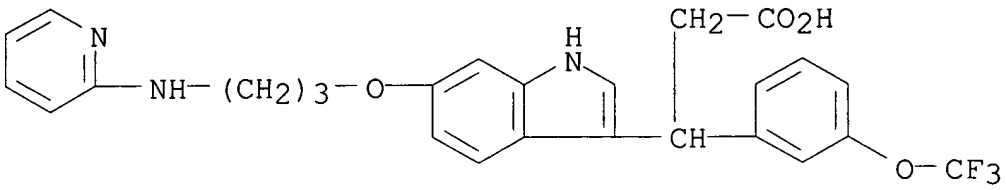
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-03-3 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-[3-(trifluoromethoxy)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

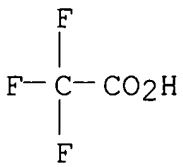
CM 1

CRN 354823-02-2
CMF C26 H24 F3 N3 O4

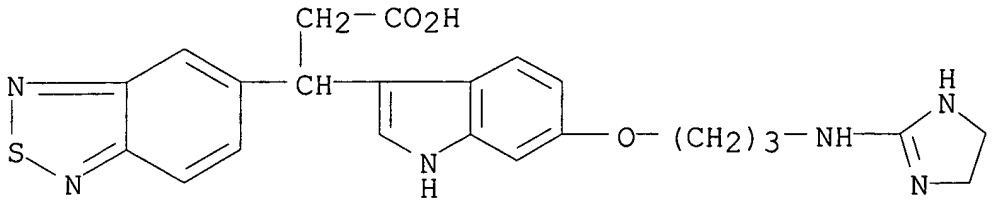


CM 2

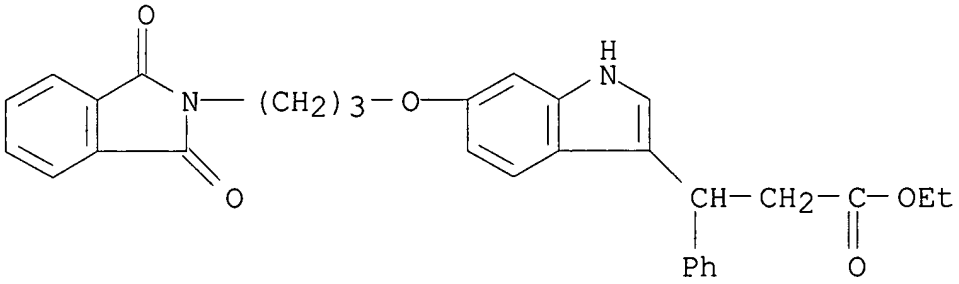
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-06-6 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)



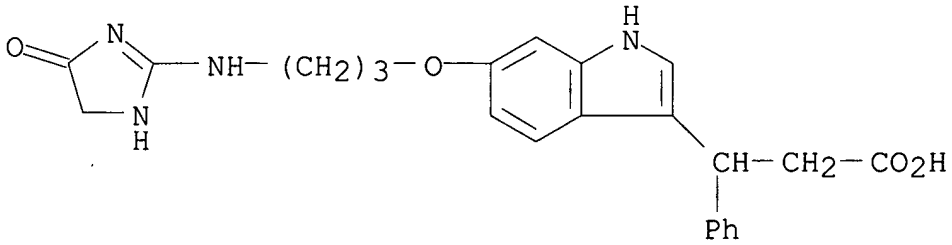
RN 354823-11-3 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)propoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 354823-18-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(4,5-dihydro-4-oxo-1H-imidazol-2-yl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

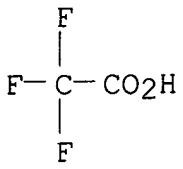
CM 1

CRN 354823-17-9
CMF C23 H24 N4 O4

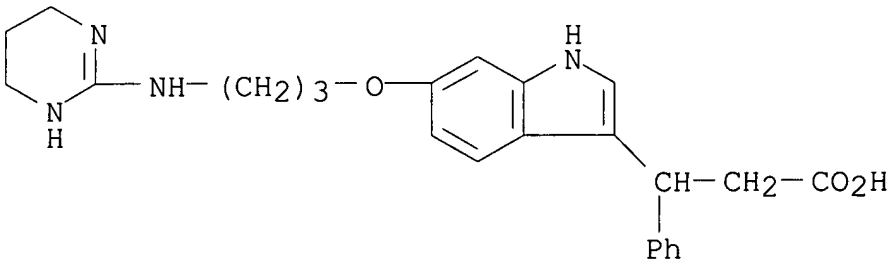


CM 2

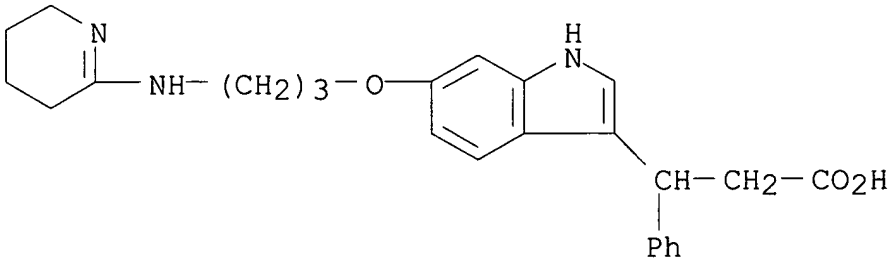
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-25-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]- (9CI) (CA INDEX NAME)



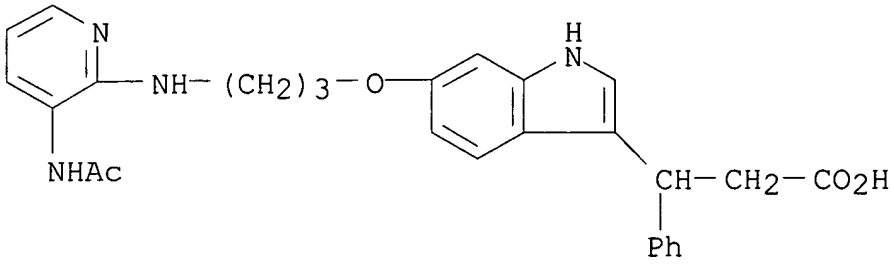
RN 354823-28-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]propoxy]- (9CI) (CA INDEX NAME)



RN 354823-43-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[[3-(acetylamino)-2-pyridinyl]amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

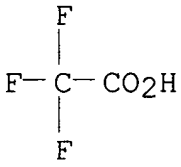
CM 1

CRN 354823-42-0
CMF C27 H28 N4 O4



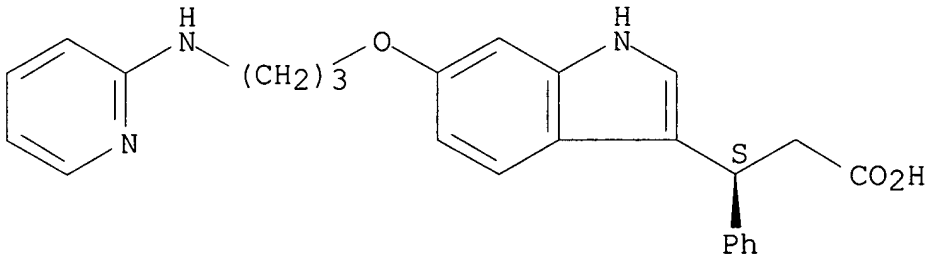
CM 2

CRN 76-05-1
CMF C2 H F3 O2



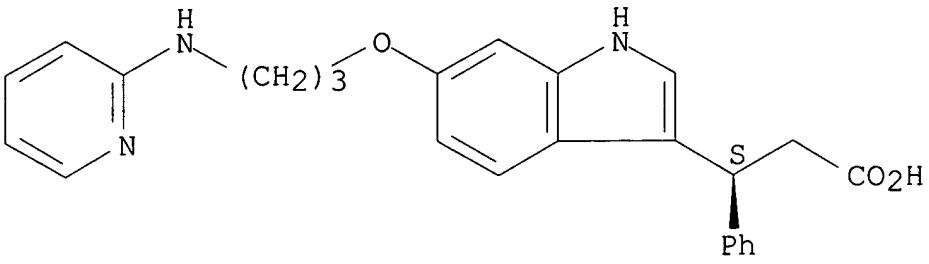
RN 354823-47-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 354823-49-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, monohydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



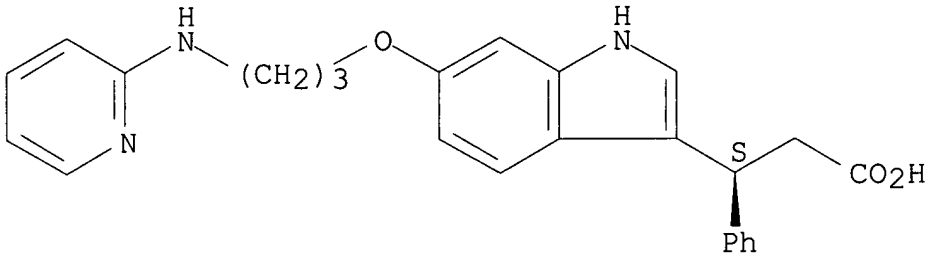
● HCl

RN 354823-52-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, (.beta.S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

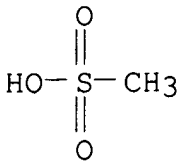
CRN 354823-47-5
CMF C25 H25 N3 O3

Absolute stereochemistry.

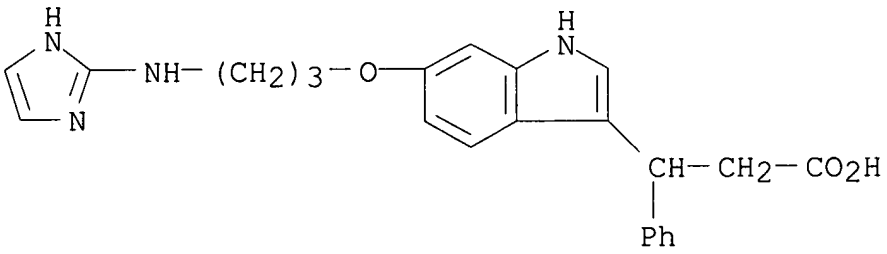


CM 2

CRN 75-75-2
CMF C H4 O3 S



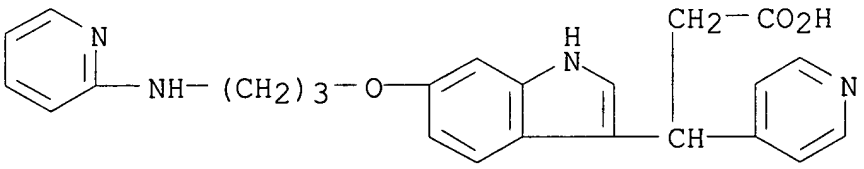
RN 354823-55-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1H-imidazol-2-ylamino)propoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



RN 724478-49-3 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-4-pyridinyl-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

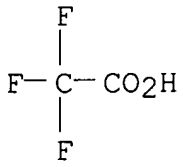
CM 1

CRN 354822-45-0
CMF C24 H24 N4 O3



CM 2

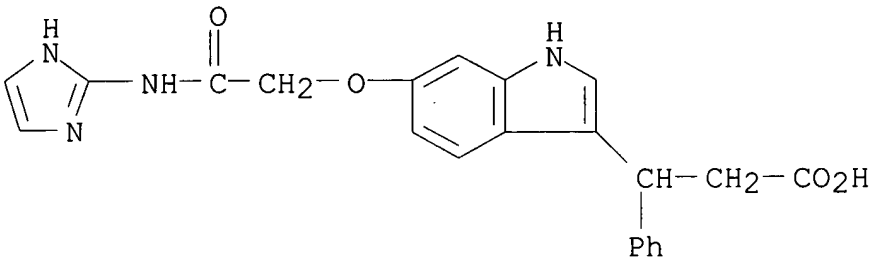
CRN 76-05-1
CMF C2 H F3 O2



RN 724478-50-6 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-imidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

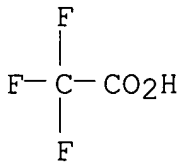
CM 1

CRN 354822-39-2
CMF C22 H20 N4 O4



CM 2

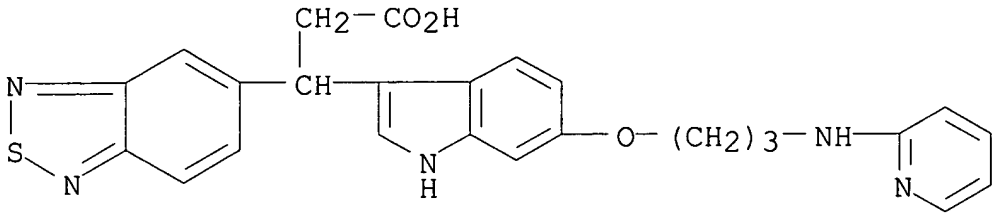
CRN 76-05-1
CMF C2 H F3 O2



RN 724478-55-1 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[3-(2-pyridinylamino)propoxy]-1H-indol-3-yl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

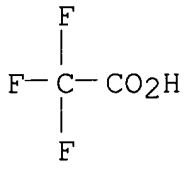
CM 1

CRN 354822-48-3
CMF C25 H23 N5 O3 S



CM 2

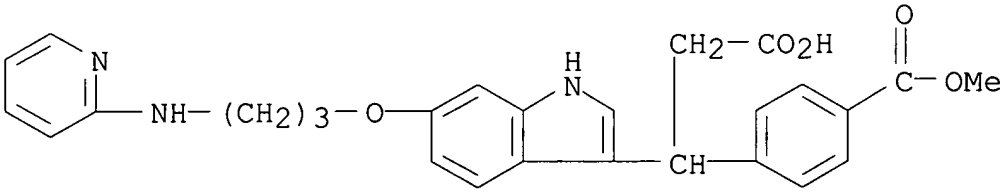
CRN 76-05-1
CMF C2 H F3 O2



RN 724478-56-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[4-(methoxycarbonyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

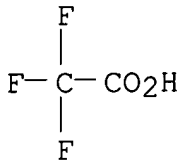
CM 1

CRN 354822-50-7
CMF C27 H27 N3 O5



CM 2

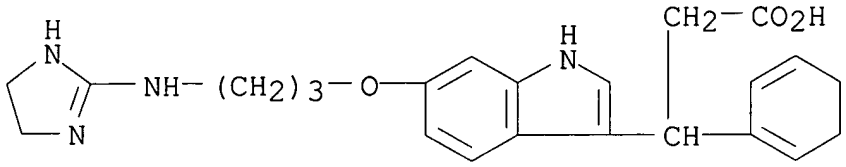
CRN 76-05-1
CMF C2 H F3 O2



RN 724478-60-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-1,5-cyclohexadien-1-yl-6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

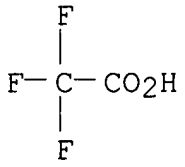
CM 1

CRN 724478-59-5
CMF C23 H28 N4 O3

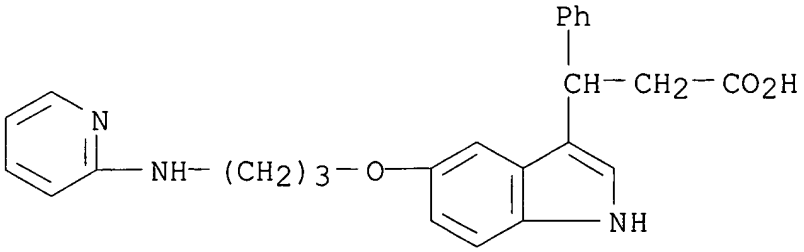


CM 2

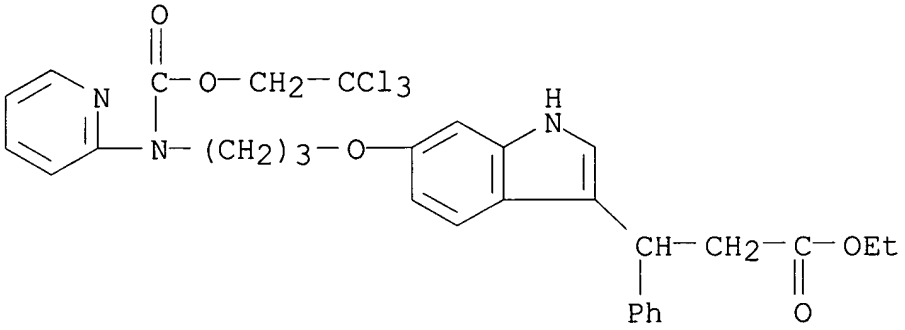
CRN 76-05-1
CMF C2 H F3 O2



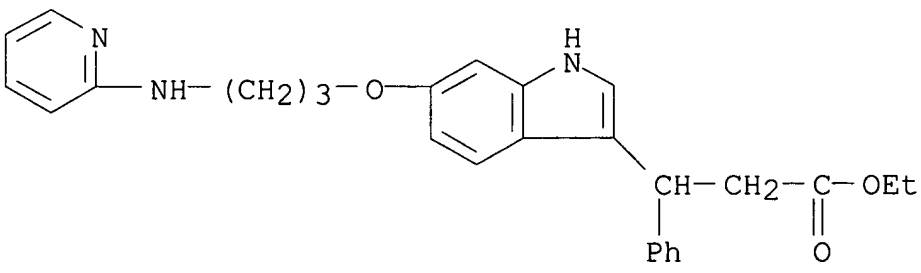
IT **354822-36-9 354822-55-2**
(prepn. of indole derivs., useful as integrin inhibitors)
RN 354822-36-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



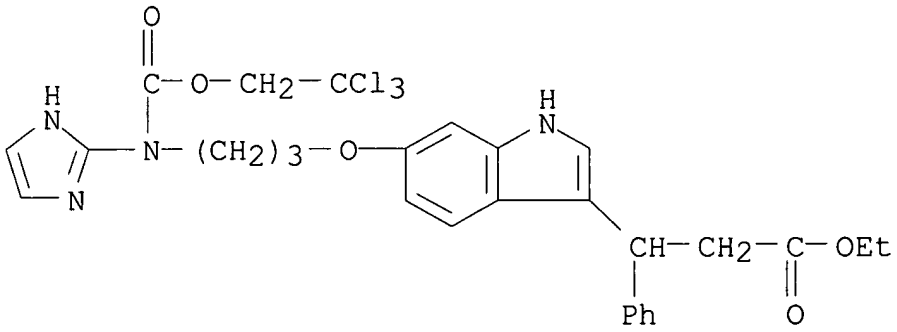
RN 354822-55-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[2-pyridinyl[(2,2,2-trichloroethoxy)carbonyl]amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



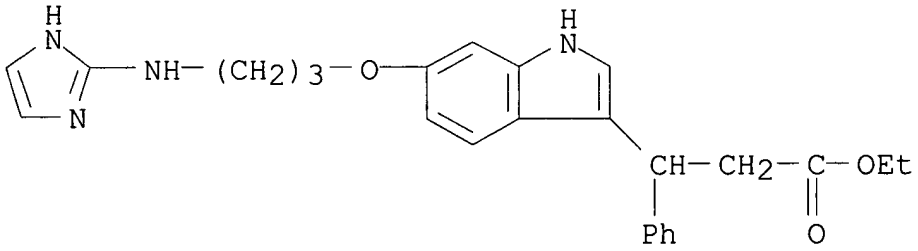
IT **354822-56-3P 354822-58-5P 354822-60-9P**
354822-66-5P 354822-67-6P 354822-74-5P
354823-19-1P 354823-21-5P 354823-23-7P
354823-26-0P 354823-38-4P 497955-40-5P
724478-54-0P 724478-62-0P
(prepn. of indole derivs., useful as integrin inhibitors)
RN 354822-56-3 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



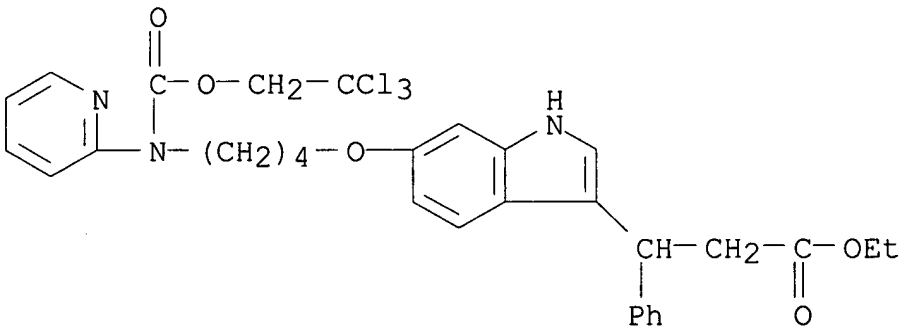
RN 354822-58-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[1H-imidazol-2-yl[(2,2,2-trichloroethoxy)carbonyl]amino]propoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



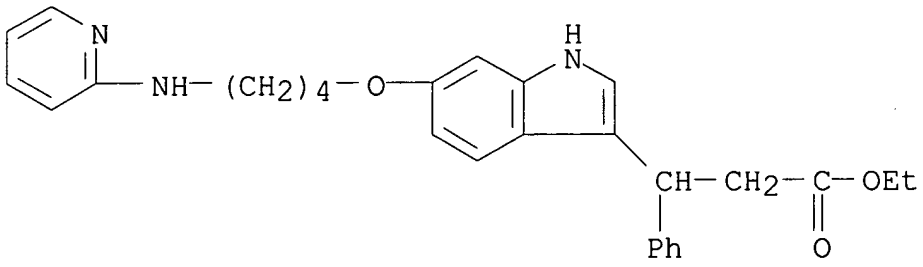
RN 354822-60-9 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1H-imidazol-2-ylamino)propoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



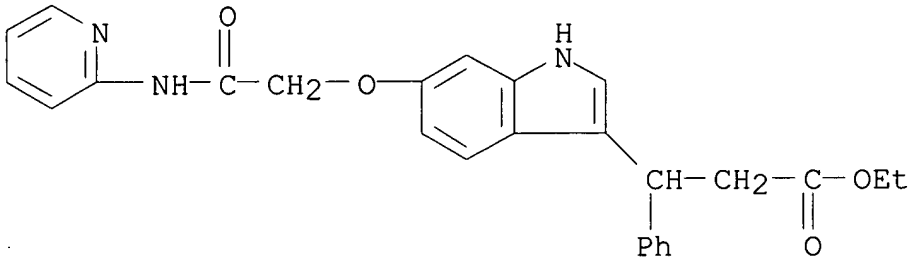
RN 354822-66-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-[2-pyridinyl[(2,2,2-trichloroethoxy)carbonyl]amino]butoxy]-, ethyl ester (9CI) (CA INDEX NAME)



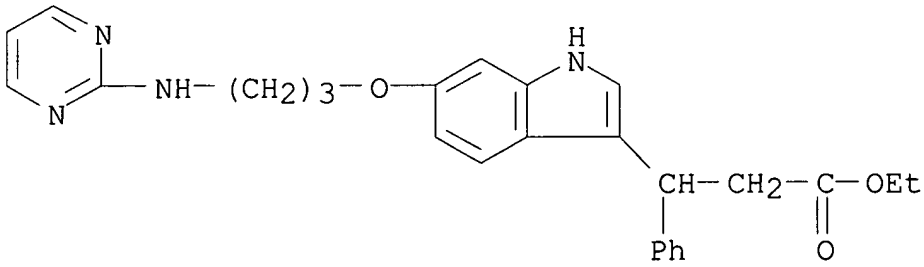
RN 354822-67-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-(2-pyridinylamino)butoxy]-, ethyl ester (9CI) (CA INDEX NAME)



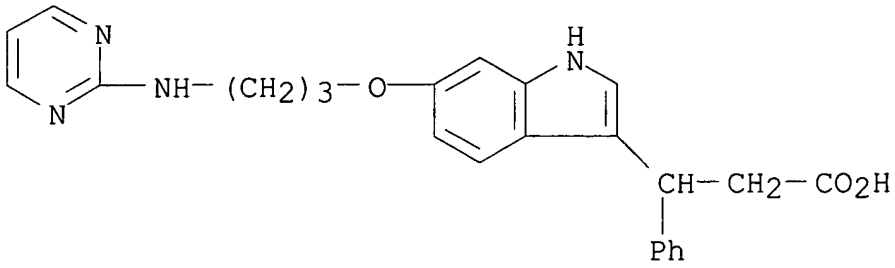
RN 354822-74-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-oxo-2-(2-pyridinylamino)ethoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



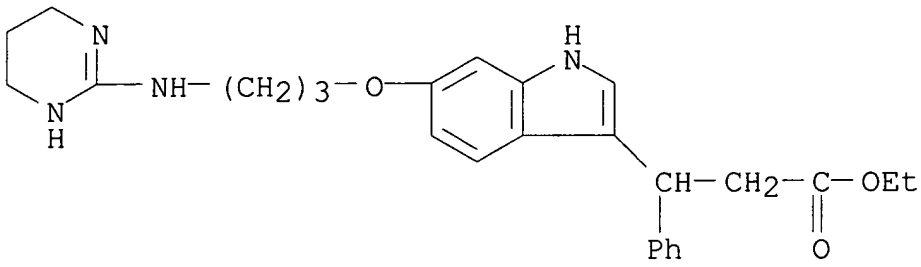
RN 354823-19-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyrimidinylamino)propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



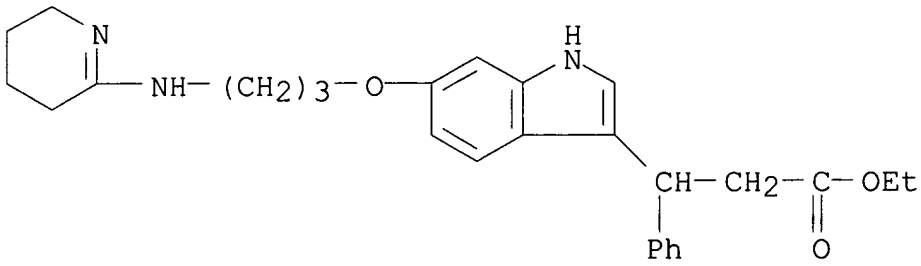
RN 354823-21-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyrimidinylamino)propoxy]- (9CI) (CA INDEX NAME)



RN 354823-23-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



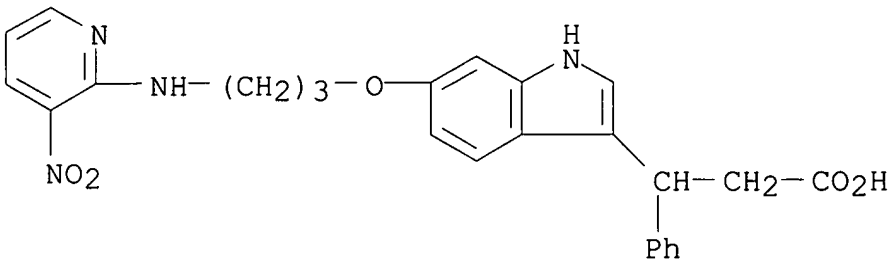
RN 354823-26-0 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 354823-38-4 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(3-nitro-2-pyridinyl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

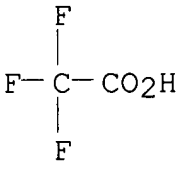
CM 1

CRN 354823-37-3
CMF C25 H24 N4 O5

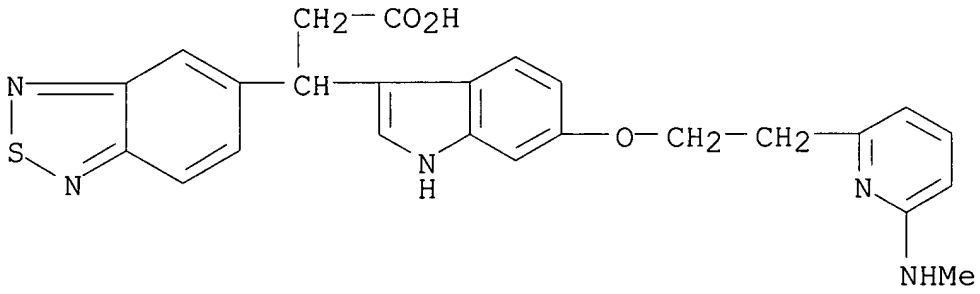


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 497955-40-5 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)

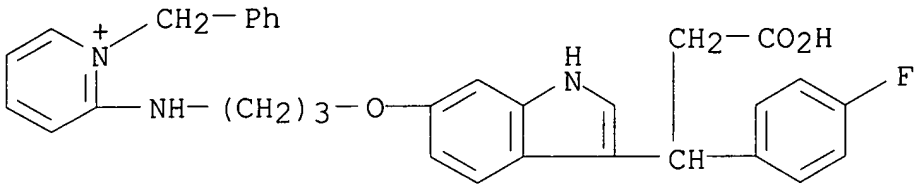


RN 724478-54-0 ZCA
CN Pyridinium, 2-[[3-[[3-[2-carboxy-1-(4-fluorophenyl)ethyl]-1H-indol-6-yl]oxy]propyl]amino]-1-(phenylmethyl)-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

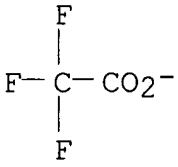
CRN 724478-53-9

CMF C32 H31 F N3 O3



CM 2

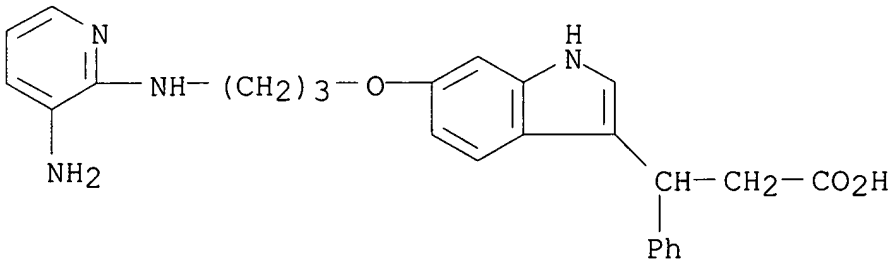
CRN 14477-72-6
CMF C2 F3 O2



RN 724478-62-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(3-amino-2-pyridinyl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 354823-39-5
CMF C25 H26 N4 O3



CM 2

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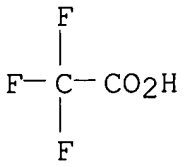

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354823-03-3P 354823-06-6P 354823-11-3P
354823-18-0P 354823-25-9P 354823-28-2P
354823-43-1P 354823-47-5P 354823-49-7P
354823-52-2P 354823-55-5P 724478-49-3P
724478-50-6P 724478-55-1P 724478-56-2P
724478-60-8P
(prepn. of indole derivs., useful as integrin inhibitors)

IT **354822-36-9 354822-55-2**
(prepn. of indole derivs., useful as integrin inhibitors)

IT **354822-56-3P 354822-58-5P 354822-60-9P**
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354823-19-1P 354823-21-5P 354823-23-7P
354823-26-0P 354823-38-4P 497955-40-5P
724478-54-0P 724478-62-0P
(prepn. of indole derivs., useful as integrin inhibitors)

L11 ANSWER 3 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:297473 ZCA
TITLE: Methods for inhibition of angiogenesis using .alpha.v.beta.3 integrin antagonists
INVENTOR(S): Brooks, Peter C.; Cheresh, David A.
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 88 pp., Cont.-in-part of U.S. Pat. Appl. 2003 176,334.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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WO 2004087057 A2 20041014 WO 2004-US9321
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WO 2004087057 A3 20060323

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EP 1613268 A2 20060111 EP 2004-758403
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PRIORITY APPLN. INFO.: US 1996-15869P P
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	US 2003-402212	A	200303 28
	WO 2004-US9321	W	200403 26

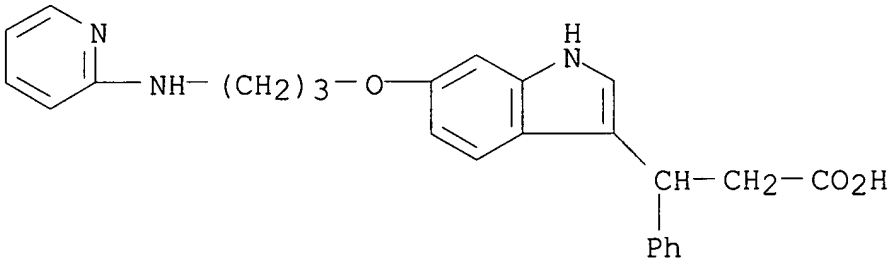
OTHER SOURCE(S): MARPAT 140:297473

AB The invention describes methods for inhibition angiogenesis in tissues using org. peptidomimetic .alpha.v.beta.3 antagonists, and particularly for inhibiting angiogenesis in inflamed tissues and in tumor tissues and metastases using therapeutic compns. contg. .alpha.v.beta.3 antagonists. The antagonists are org. compds. having a basic group and an acidic group spaced from one another by a distance in the range of about 10 Angstroms to about 100 Angstroms, as described in detail herein.

IT **354822-33-6 354823-47-5 497955-40-5**

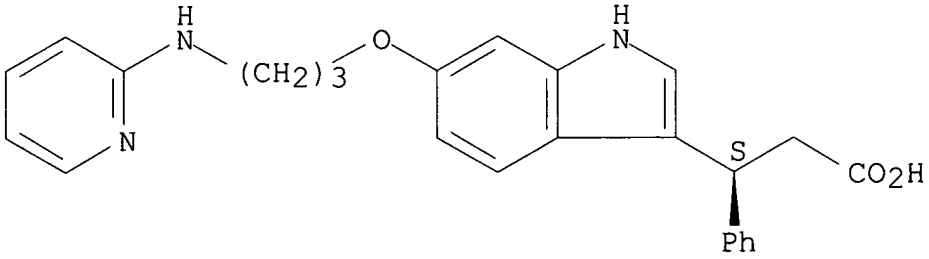
(methods for inhibition of angiogenesis using .alpha.v.beta.3 integrin antagonists)

RN 354822-33-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

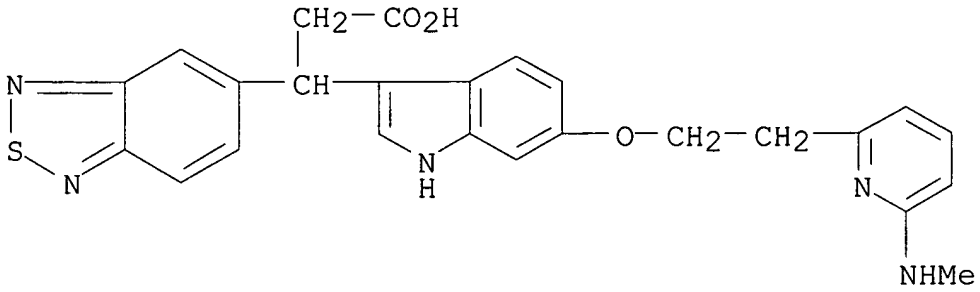


RN 354823-47-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 497955-40-5 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[2-[6-(methylamino)-2-pyridinyl]ethoxy]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)



IT **354822-33-6 354823-47-5 497955-40-5**
(methods for inhibition of angiogenesis using .alpha.v.beta.3 integrin antagonists)

L11 ANSWER 4 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:118447 ZCA
TITLE: Preparation of benzimidazolecarboxylates and related compounds as viral polymerase inhibitors
INVENTOR(S): Beaulieu, Pierre Louis; Fazal, Gulrez; Gillard, James; Kukolj, George; Austel, Volkhard
PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004425	A2	20020117	WO 2001-CA989	20010704
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WO 2002070739 A2 20020912 WO 2002-CA323
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WO 2002070739 A3 20030530
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EP 1370682 A2 20031217 EP 2002-712681
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US 2004224955 A1 20041111 US 2004-851710
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PRIORITY APPLN. INFO.:

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WO 2001-CA989	W	200107 04
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OTHER SOURCE(S): MARPAT 136:118447

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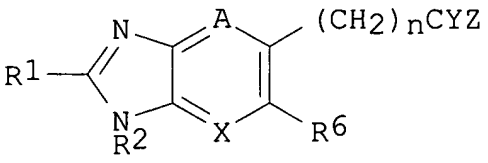


I

AB Title compds. [I; X = CH, N; Y = O, S; Z = OH, NH2, NMeR3, NHR3, OR3, 5-6 membered (substituted) heterocyclyl; A = N, COR7, CR5; R5 =

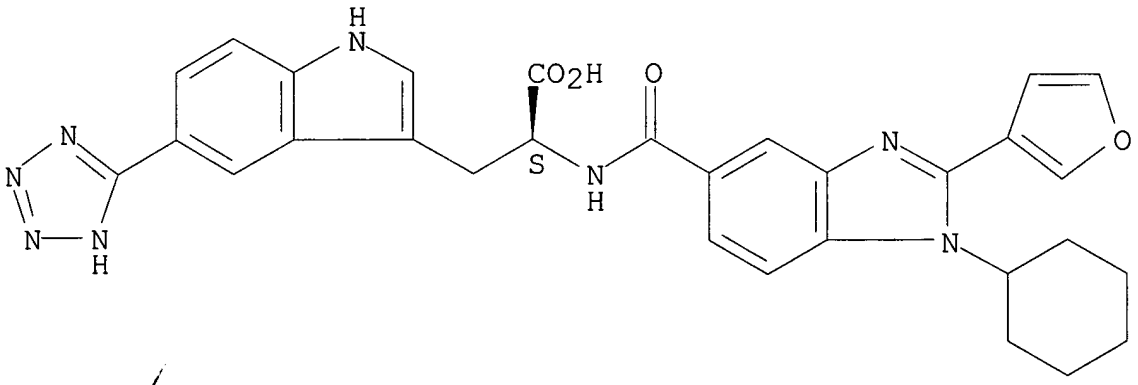
H, halo, alkyl; R7 = H, alkyl; X and A are not both N; R6 = H, halo, alkyl, OR7; R7 = H , alkyl; R1 = (substituted) hetero(bi)cyclyl, Ph, phenylalkyl, alkenyl, phenylalkenyl, cycloalkyl, alkyl, CF3; R2 = (substituted) alkyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, adamantyl, Ph, pyridyl; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, alkenyl, cycloalkylalkenyl, arylalkenyl, dialkylamino, heterocyclyl, etc.; n = 0, 1], were prepd. Thus, Me 3-amino-4-cyclohexylaminobenzoate (prepn. given), 2-pyridinecarboxaldehyde, and Oxone were stirred in DMF to give 80% Et 1-cyclohexyl-2-pyridin-2-yl-1H-benzimidazole-5-carboxylate, which was sapond. with aq. NaOH in MeOH to give 91% 1-cyclohexyl-2-pyridin-2-yl-1H-benzimidazole-5-carboxylic acid. The latter inhibited hepatitis C virus RNA dependent polymerase (NS5B) with IC50 = 1-5 .mu.M.

IT **390809-91-3P**
(prepn. of benzimidazolecarboxylates and related compds. as viral polymerase inhibitors)

RN 390809-91-3 ZCA

CN L-Tryptophan, N-[[1-cyclohexyl-2-(3-furanyl)-1H-benzimidazol-5-yl]carbonyl]-5-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **390809-91-3P**
(prepn. of benzimidazolecarboxylates and related compds. as viral polymerase inhibitors)

L11 ANSWER 5 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 135:180700 ZCA

TITLE: Preparation of indol-3-ylpropionates as integrin inhibitors.

INVENTOR(S): Goodman, Simon; Gottschlich, Rudolf; Wiesner, Matthias

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058893	A2	20010816	WO 2001-EP84	20010105
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WO 2001058893	A3	20020418		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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OTHER SOURCE(S): MARPAT 135:180700

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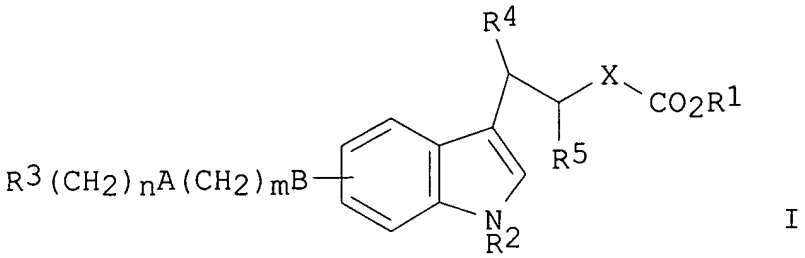


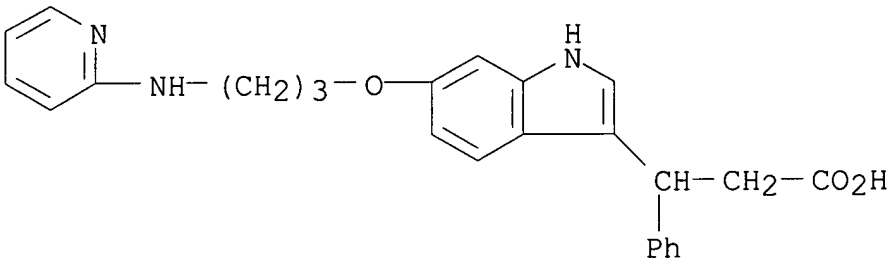
I

AB Title compds. [I; A, B = O, S, NH, NR7, CO, CONH, bond; X = (substituted) alkylene; R1 = H, Z, (CH2)oAr; R2 = H, R7, COZ; R3 = NHR6, NR6C(:NR6)NHR6, Het; R4, R5 = H, O, R7, (CH2)oAr, OAr, etc.; R6 = H, COR7, COAr, R7, CO2R7, SO2R7, etc.; R7 = alkyl, cycloalkyl; Z = alkyl; Ar = (substituted) aryl; Het = (unsatd.) (substituted) mono- or bicyclic N-heterocyclyl; m = 0-6; n, o = 0-2], were prepd. as integrin inhibitors useful for combating thrombosis, myocardial infarcts, coronary heart disease, arteriosclerosis, inflammation, tumors, osteoporosis, rheumatic arthritis, macular degenerative diseases, diabetic retinopathy, infections, restenosis after angioplasty, and pathol. conditions which are maintained or propagated by angiogenesis (no data). Thus, 6-benzyloxyindole, PhCHO, Meldrum's acid, and L-proline were stirred 3 h in MeCN to give 5-[phenyl-(6-O-benzylindol-3-yl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione. The latter was refluxed with Cu powder in pyridine/EtOH to give Et 3-phenyl-3-(6-O-benzylindol-3-yl)propionate, which was hydrogenated in EtOH over Pd/C to give Et 3-phenyl-3-(6-hydroxyindol-3-yl)propionate. This was converted to 3-phenyl-3-[6-[3-(pyridin-2-ylamino)propoxy]indol-3-yl]propionic acid in several steps.

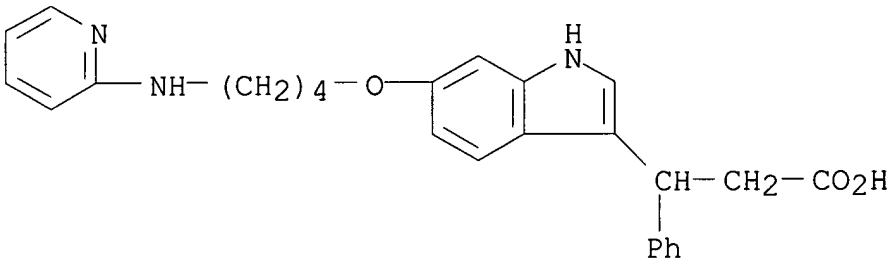
IT **354822-33-6P 354822-34-7P 354822-35-8P**
354822-36-9P 354822-37-0P 354822-38-1P
354822-39-2P 354822-40-5P 354822-41-6P
354822-42-7P 354822-43-8P 354822-44-9P
354822-45-0P 354822-46-1P 354822-48-3P
354822-49-4P 354822-50-7P 354822-62-1P

354822-63-2P 354822-68-7P 354822-69-8P
354822-70-1P 354822-75-6P 354822-83-6P
354822-85-8P 354822-86-9P 354822-88-1P
354822-89-2P 354822-90-5P 354822-91-6P
354822-93-8P 354822-95-0P 354822-97-2P
354823-01-1P 354823-03-3P 354823-07-7P
354823-08-8P 354823-10-2P 354823-18-0P
354823-21-5P 354823-25-9P 354823-28-2P
354823-47-5P 354823-49-7P 354823-52-2P
354823-56-6P 354823-71-5P
(prepn. of indolylpropionates as integrin inhibitors)

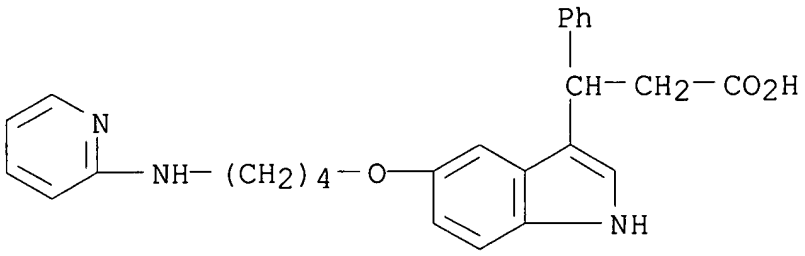
RN 354822-33-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



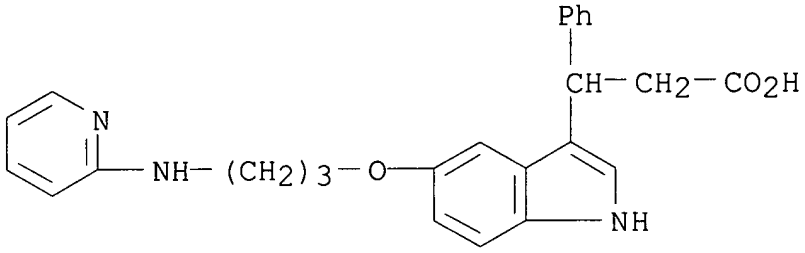
RN 354822-34-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-(2-pyridinylamino)butoxy]- (9CI) (CA INDEX NAME)



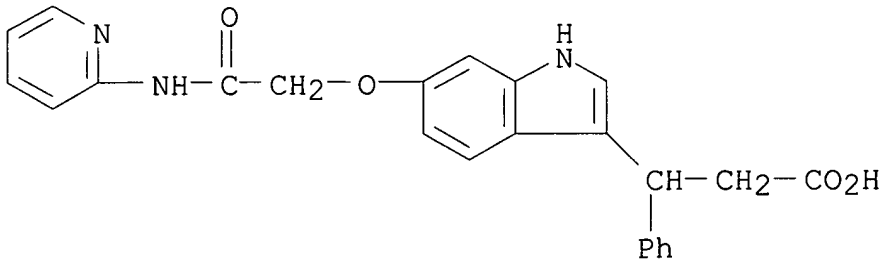
RN 354822-35-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[4-(2-pyridinylamino)butoxy]- (9CI) (CA INDEX NAME)



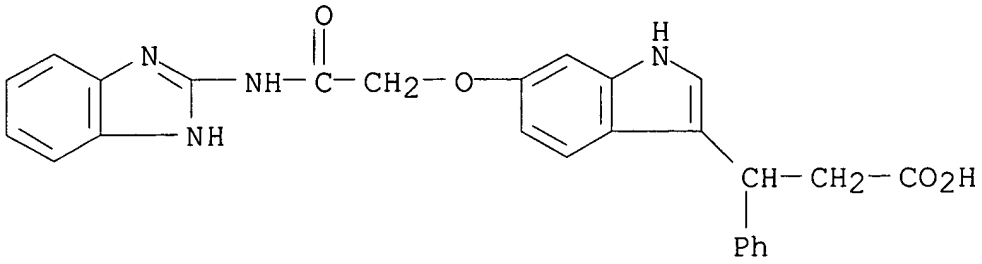
RN 354822-36-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



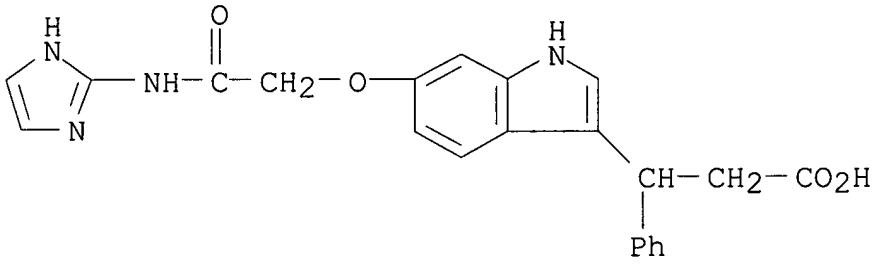
RN 354822-37-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-oxo-2-(2-pyridinylamino)ethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



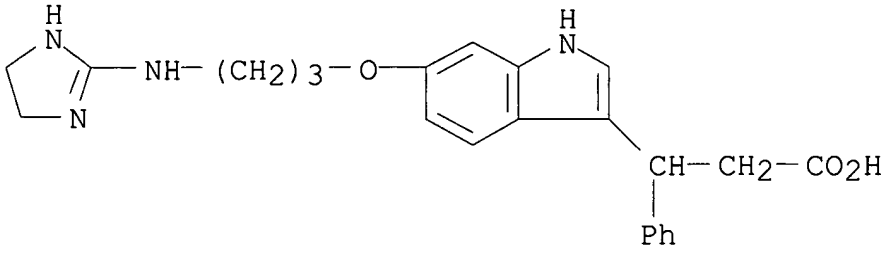
RN 354822-38-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-benzimidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



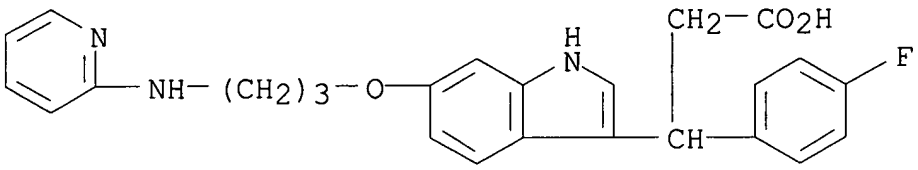
RN 354822-39-2 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-imidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)



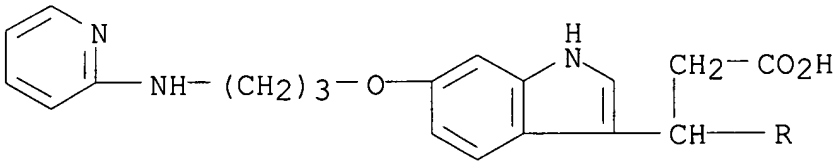
RN 354822-40-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-.beta.-phenyl- (9CI) (CA INDEX NAME)

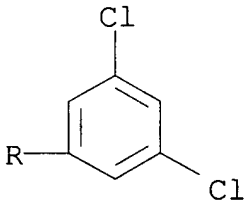


RN 354822-41-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(4-fluorophenyl)-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

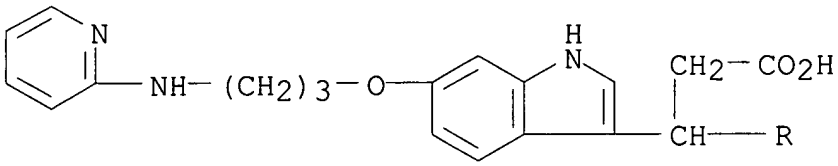


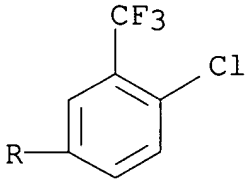
RN 354822-42-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3,5-dichlorophenyl)-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



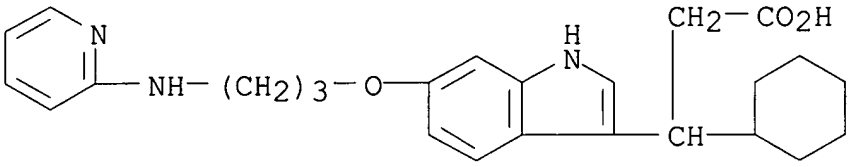


RN 354822-43-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[4-chloro-3-(trifluoromethyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

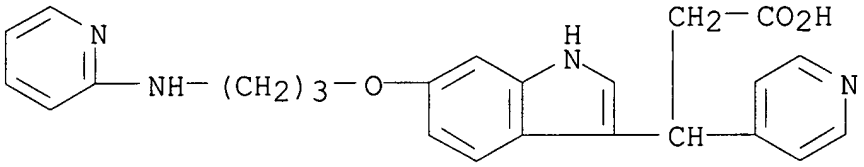




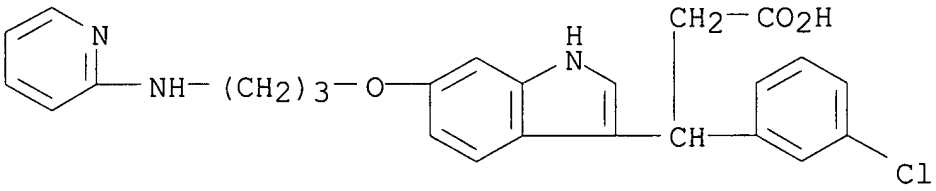
RN 354822-44-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-cyclohexyl-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



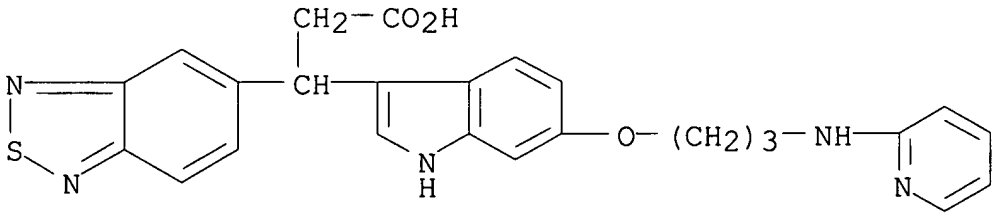
RN 354822-45-0 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-4-pyridinyl-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



RN 354822-46-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3-chlorophenyl)-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)

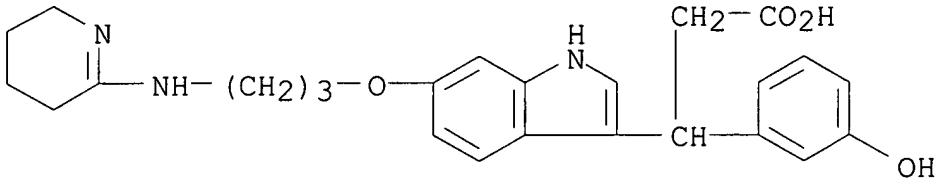


RN 354822-48-3 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[3-(2-pyridinylamino)propoxy]-1H-indol-3-yl]- (9CI) (CA INDEX NAME)

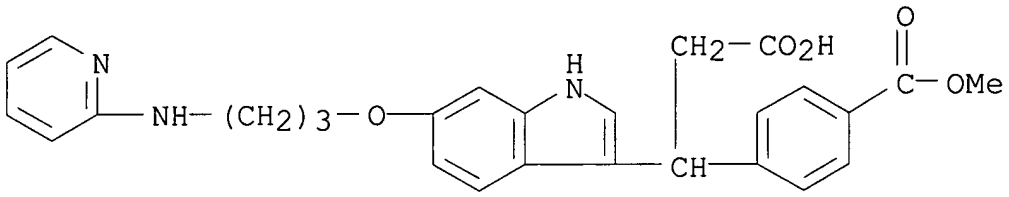


RN 354822-49-4 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3-hydroxyphenyl)-6-[3-[(3,4,5,6-

tetrahydro-2-pyridinyl)amino]propoxy]- (9CI) (CA INDEX NAME)



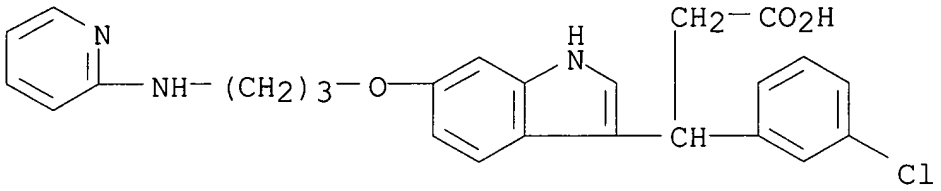
RN 354822-50-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[4-(methoxycarbonyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]- (9CI) (CA INDEX NAME)



RN 354822-62-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(3-chlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

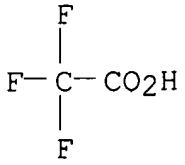
CM 1

CRN 354822-46-1
CMF C25 H24 Cl N3 O3



CM 2

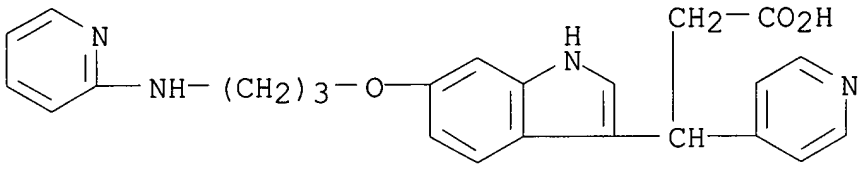
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-63-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-4-pyridinyl-6-[3-(2-pyridinylamino)propoxy]-, trifluoroacetate (9CI) (CA INDEX NAME)

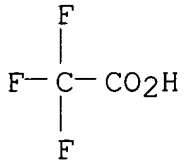
CM 1

CRN 354822-45-0
CMF C24 H24 N4 O3



CM 2

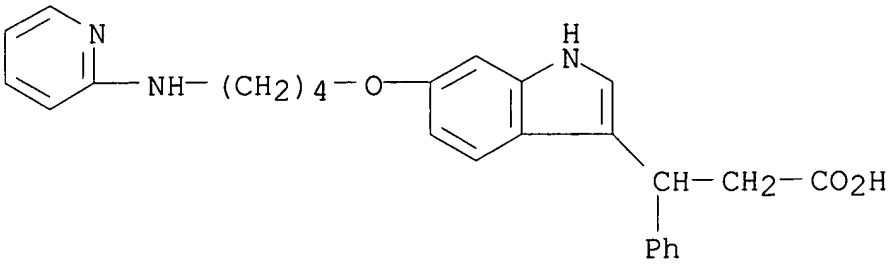
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-68-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-(2-pyridinylamino)butoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

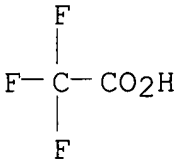
CM 1

CRN 354822-34-7
CMF C26 H27 N3 O3



CM 2

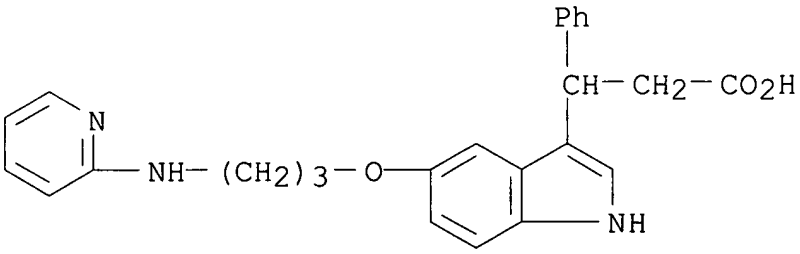
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-69-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

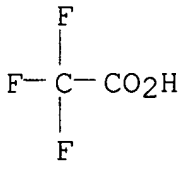
CRN 354822-36-9
CMF C25 H25 N3 O3



CM 2

CRN 76-05-1

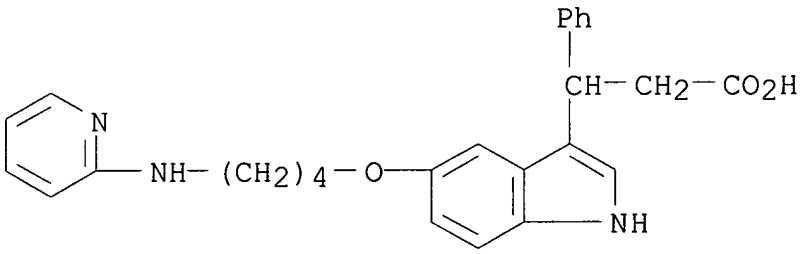
CMF C2 H F3 O2



RN 354822-70-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-5-[4-(2-pyridinylamino)butoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

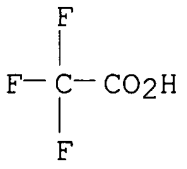
CM 1

CRN 354822-35-8
CMF C26 H27 N3 O3



CM 2

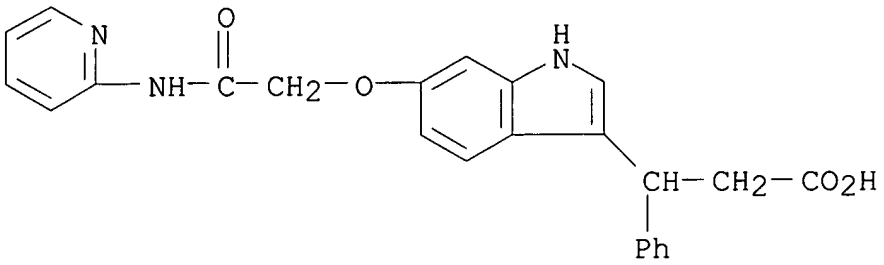
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-75-6 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-oxo-2-(2-pyridinylamino)ethoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

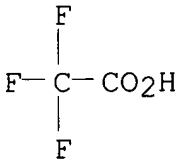
CM 1

CRN 354822-37-0
CMF C24 H21 N3 O4



CM 2

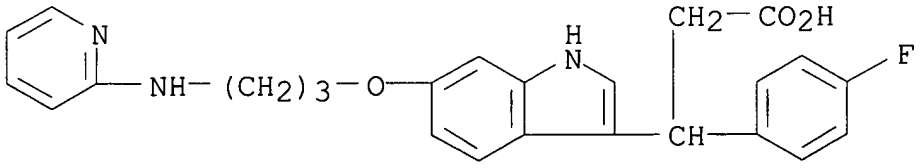
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-83-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(4-fluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

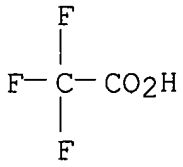
CM 1

CRN 354822-41-6
CMF C25 H24 F N3 O3



CM 2

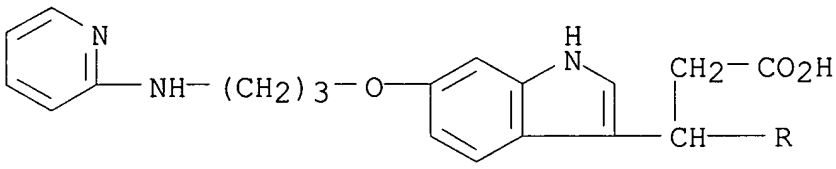
CRN 76-05-1
CMF C2 H F3 O2

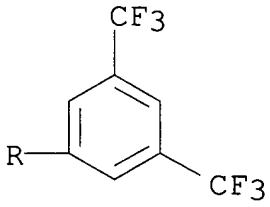


RN 354822-85-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[3,5-bis(trifluoromethyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

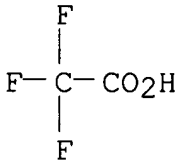
CRN 354822-84-7
CMF C27 H23 F6 N3 O3





CM 2

CRN 76-05-1
CMF C2 H F3 O2

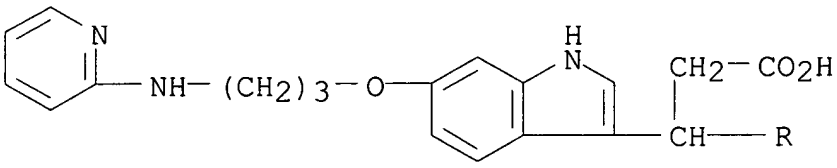


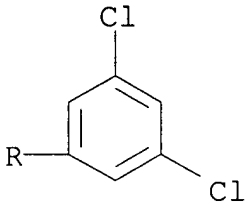
RN 354822-86-9 ZCA

CN 1H-Indole-3-propanoic acid, .beta.-(3,5-dichlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

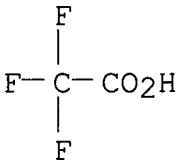
CRN 354822-42-7
CMF C25 H23 Cl2 N3 O3





CM 2

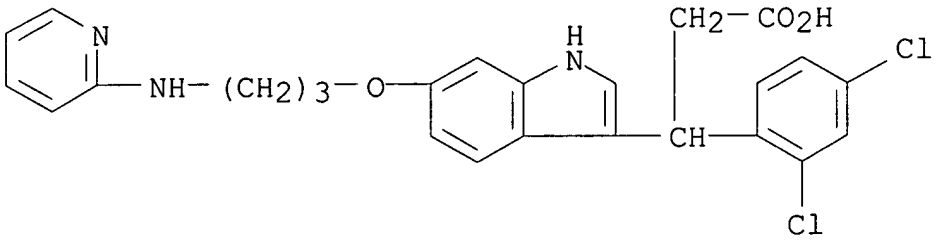
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-88-1 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2,4-dichlorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

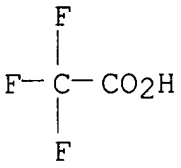
CM 1

CRN 354822-87-0
CMF C25 H23 Cl2 N3 O3



CM 2

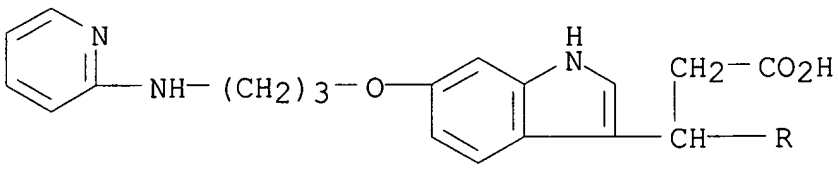
CRN 76-05-1
CMF C2 H F3 O2

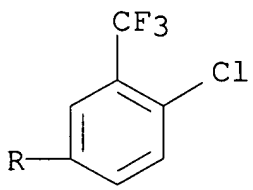


RN 354822-89-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-[4-chloro-3-(trifluoromethyl)phenyl]-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

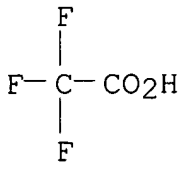
CRN 354822-43-8
CMF C26 H23 Cl F3 N3 O3





CM 2

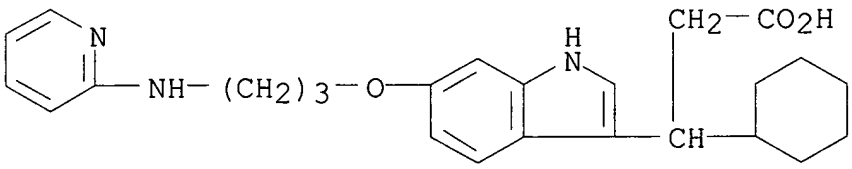
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-90-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-cyclohexyl-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

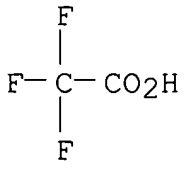
CM 1

CRN 354822-44-9
CMF C25 H31 N3 O3



CM 2

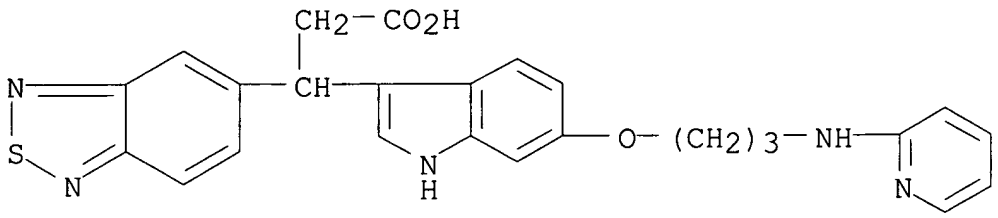
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-91-6 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[3-(2-pyridinylamino)propoxy]-1H-indol-3-yl]-, trifluoroacetate (9CI) (CA INDEX NAME)

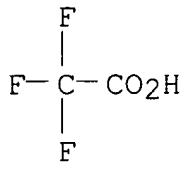
CM 1

CRN 354822-48-3
CMF C25 H23 N5 O3 S



CM 2

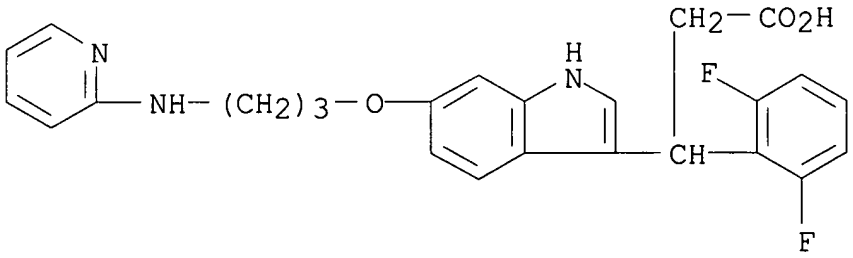
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-93-8 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2,6-difluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

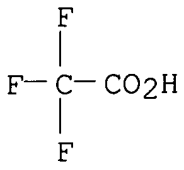
CM 1

CRN 354822-92-7
CMF C25 H23 F2 N3 O3



CM 2

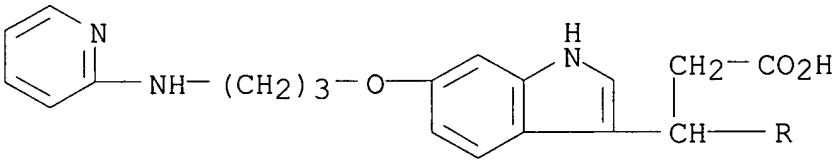
CRN 76-05-1
CMF C2 H F3 O2

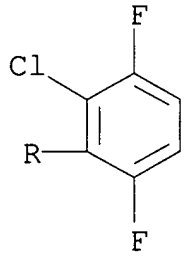


RN 354822-95-0 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(2-chloro-3,6-difluorophenyl)-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

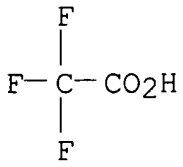
CRN 354822-94-9
CMF C25 H22 Cl F2 N3 O3





CM 2

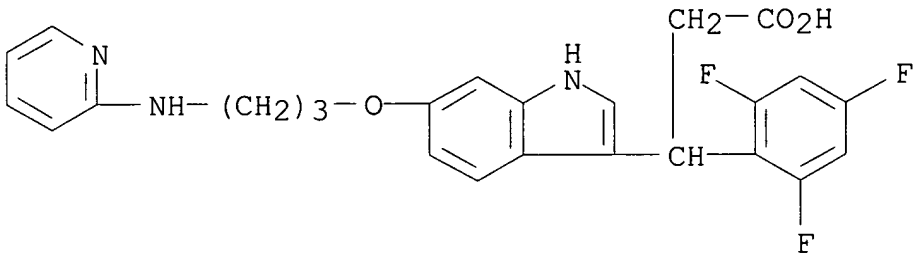
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-97-2 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-(2,4,6-trifluorophenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

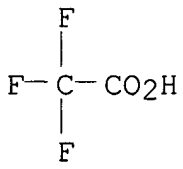
CM 1

CRN 354822-96-1
CMF C25 H22 F3 N3 O3



CM 2

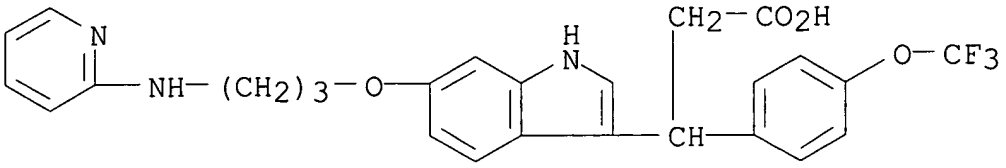
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-01-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-[4-(trifluoromethoxy)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

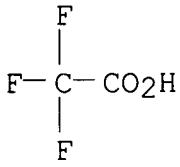
CM 1

CRN 354823-00-0
CMF C26 H24 F3 N3 O4



CM 2

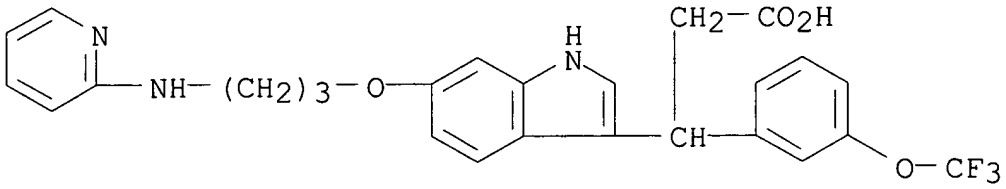
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-03-3 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(2-pyridinylamino)propoxy]-.beta.-[3-(trifluoromethoxy)phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

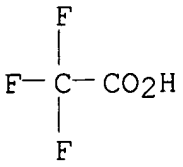
CM 1

CRN 354823-02-2
CMF C26 H24 F3 N3 O4



CM 2

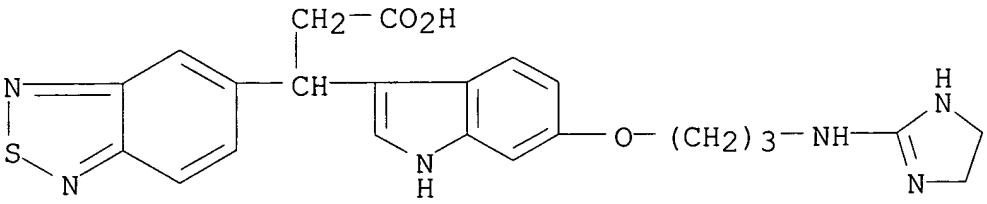
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-07-7 ZCA
CN 2,1,3-Benzothiadiazole-5-propanoic acid, .beta.-[6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-1H-indol-3-yl]-, trifluoroacetate (9CI) (CA INDEX NAME)

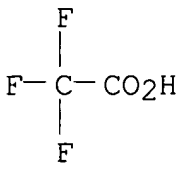
CM 1

CRN 354823-06-6
CMF C23 H24 N6 O3 S



CM 2

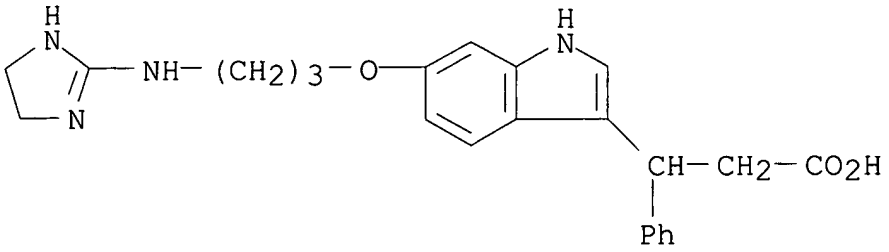
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-08-8 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

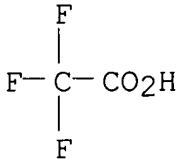
CM 1

CRN 354822-40-5
CMF C23 H26 N4 O3



CM 2

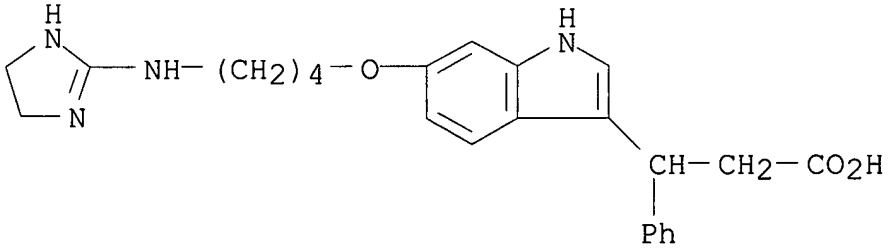
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-10-2 ZCA
CN 1H-Indole-3-propanoic acid, 6-[4-[(4,5-dihydro-1H-imidazol-2-yl)amino]butoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

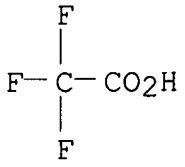
CRN 354823-09-9
CMF C24 H28 N4 O3



CM 2

CRN 76-05-1

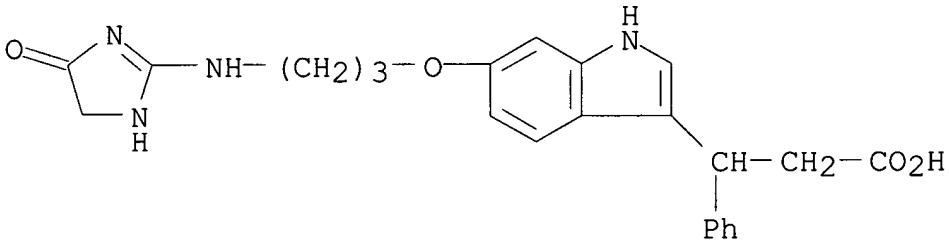
CMF C2 H F3 O2



RN 354823-18-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(4,5-dihydro-4-oxo-1H-imidazol-2-yl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

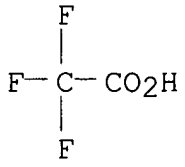
CM 1

CRN 354823-17-9
CMF C23 H24 N4 O4

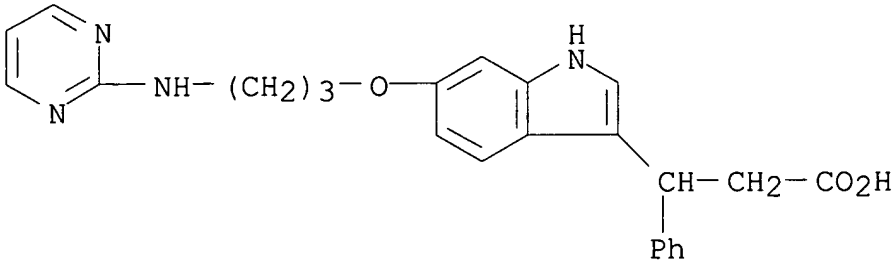


CM 2

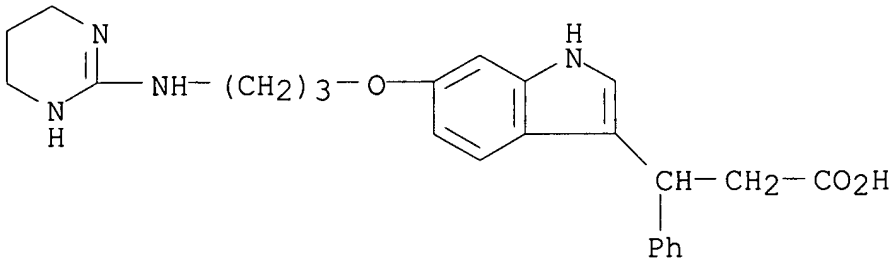
CRN 76-05-1
CMF C2 H F3 O2



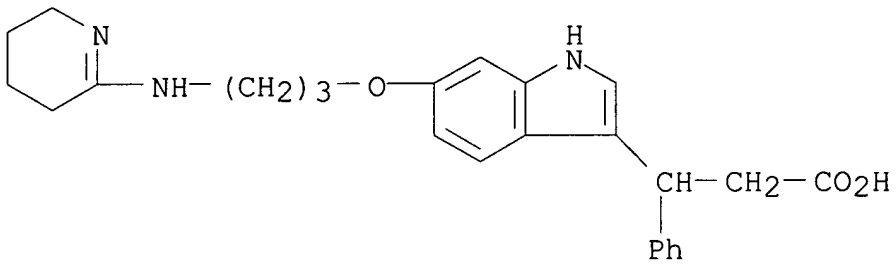
RN 354823-21-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyrimidinylamino)propoxy]- (9CI) (CA INDEX NAME)



RN 354823-25-9 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]- (9CI) (CA INDEX NAME)

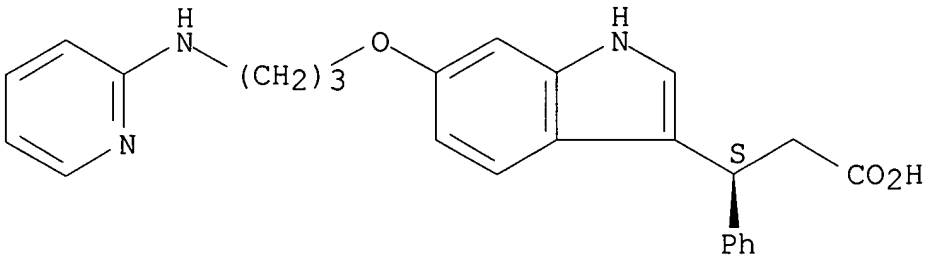


RN 354823-28-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]propoxy]- (9CI) (CA INDEX NAME)



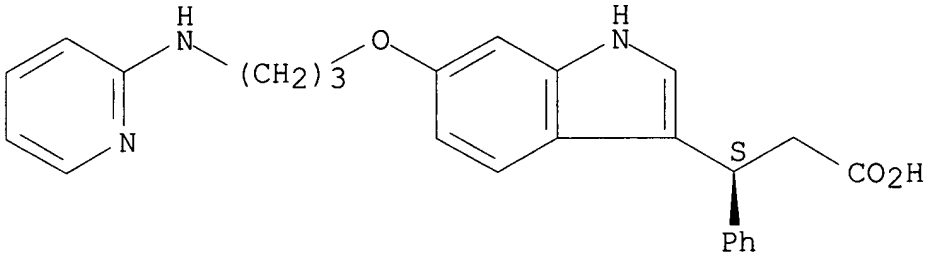
RN 354823-47-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 354823-49-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, monohydrochloride, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



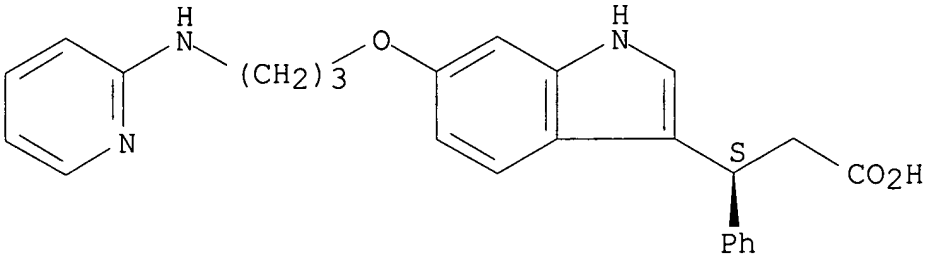
● HCl

RN 354823-52-2 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, (.beta.S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

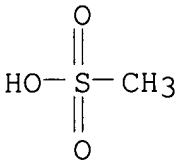
CRN 354823-47-5
CMF C25 H25 N3 O3

Absolute stereochemistry.



CM 2

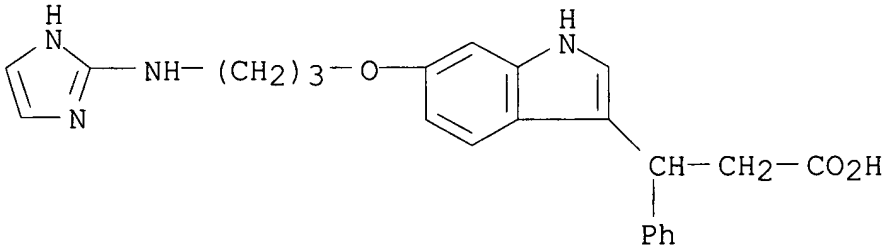
CRN 75-75-2
CMF C H4 O3 S



RN 354823-56-6 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1H-imidazol-2-ylamino)propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

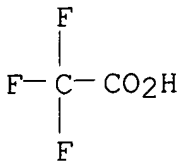
CM 1

CRN 354823-55-5
CMF C23 H24 N4 O3



CM 2

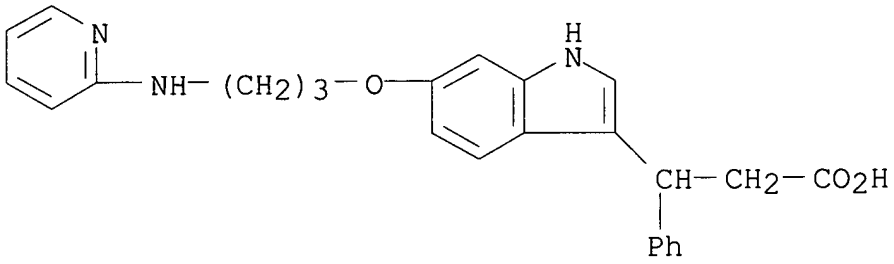
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-71-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

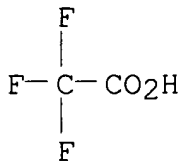
CM 1

CRN 354822-33-6
CMF C25 H25 N3 O3



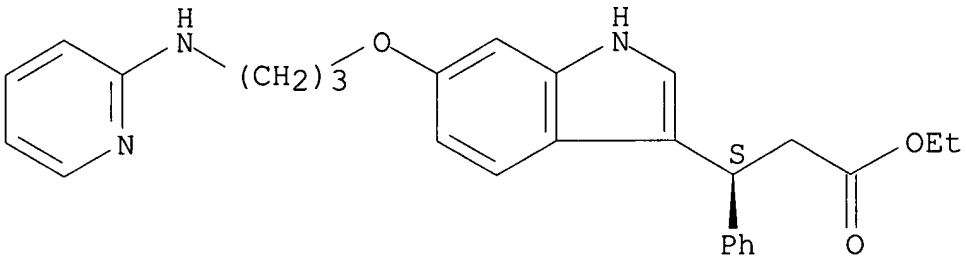
CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **354823-46-4P**
(prepn. of indolylpropionates as integrin inhibitors)
RN 354823-46-4 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

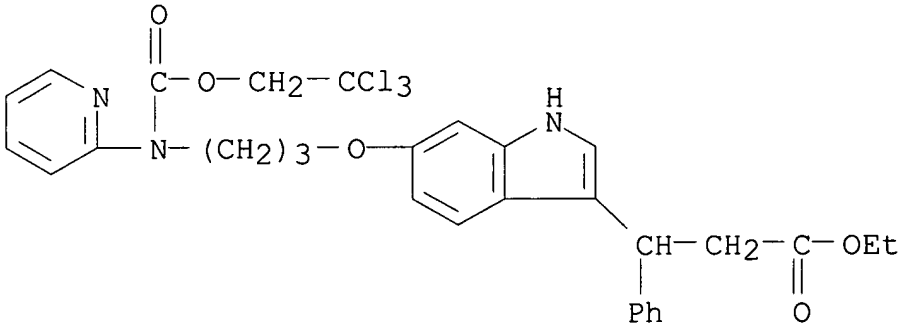
Absolute stereochemistry.



IT **354822-55-2P 354822-57-4P 354822-59-6P**
354822-61-0P 354822-66-5P 354822-67-6P
354822-74-5P 354822-76-7P 354822-82-5P
354823-11-3P 354823-20-4P 354823-23-7P
354823-26-0P 354823-38-4P 354823-40-8P
354823-43-1P
(prepn. of indolylpropionates as integrin inhibitors)

RN 354822-55-2 ZCA

CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[2-pyridinyl[(2,2,2-trichloroethoxy)carbonyl]amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)

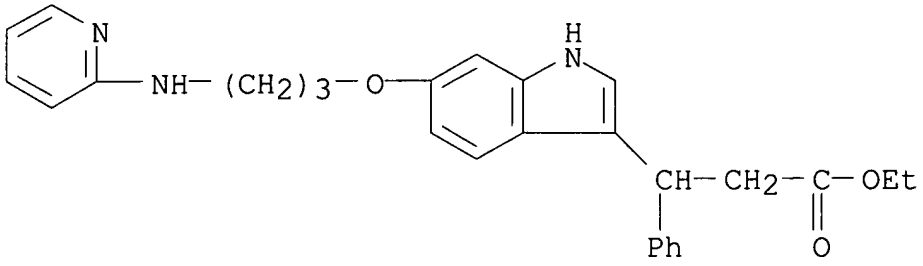


RN 354822-57-4 ZCA

CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyridinylamino)propoxy]-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

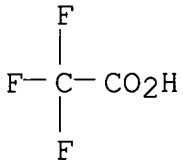
CM 1

CRN 354822-56-3
CMF C27 H29 N3 O3



CM 2

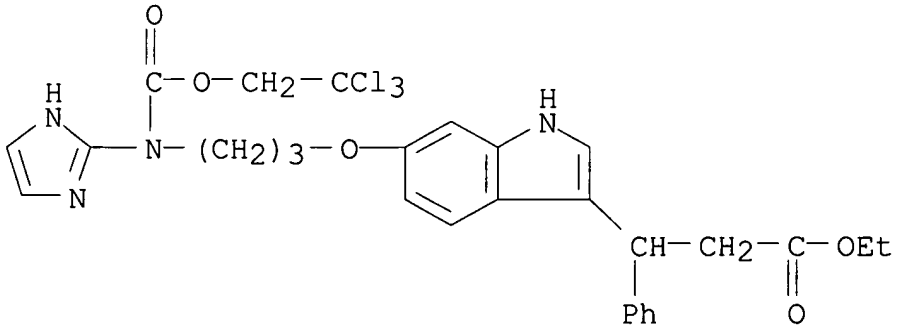
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-59-6 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[1H-imidazol-2-yl[(2,2,2-trichloroethoxy)carbonyl]amino]propoxy]-.beta.-phenyl-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

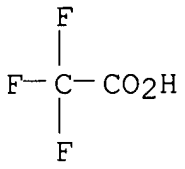
CM 1

CRN 354822-58-5
CMF C28 H29 Cl3 N4 O5



CM 2

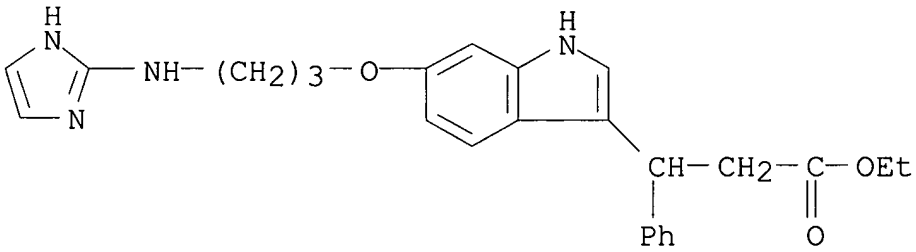
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-61-0 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1H-imidazol-2-ylamino)propoxy]-.beta.-phenyl-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

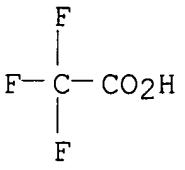
CM 1

CRN 354822-60-9
CMF C25 H28 N4 O3

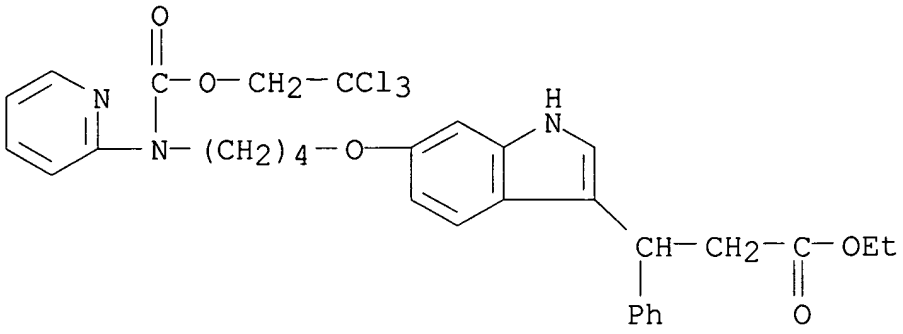


CM 2

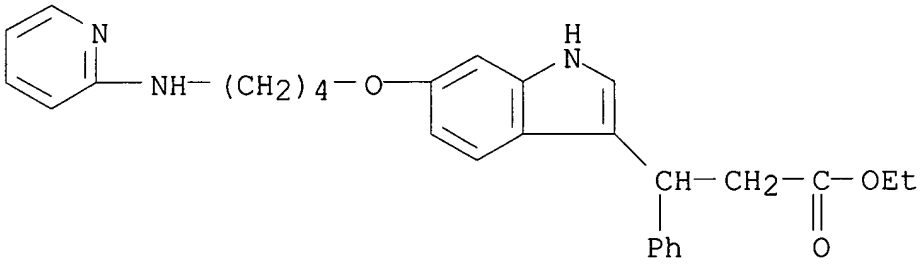
CRN 76-05-1
CMF C2 H F3 O2



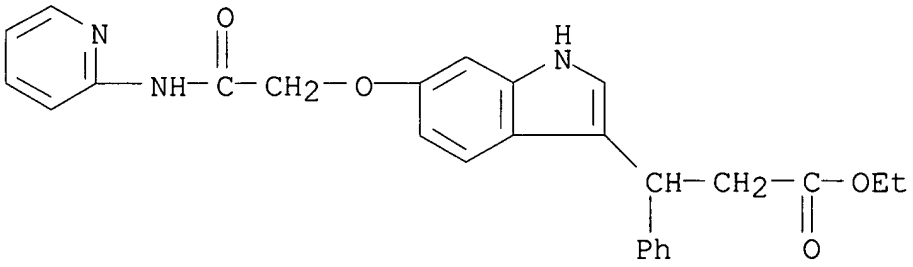
RN 354822-66-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-[2-pyridinyl[(2,2,2-trichloroethoxy)carbonyl]amino]butoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 354822-67-6 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[4-(2-pyridinylamino)butoxy]-, ethyl ester (9CI) (CA INDEX NAME)



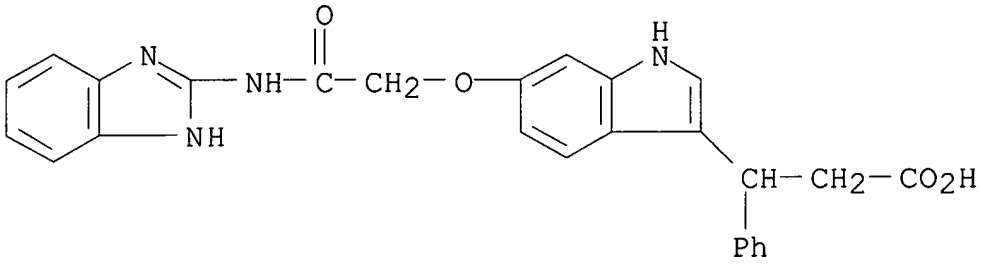
RN 354822-74-5 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-oxo-2-(2-pyridinylamino)ethoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 354822-76-7 ZCA
CN 1H-Indole-3-propanoic acid, 6-[2-(1H-benzimidazol-2-ylamino)-2-oxoethoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

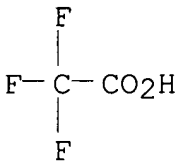
CM 1

CRN 354822-38-1
CMF C26 H22 N4 O4



CM 2

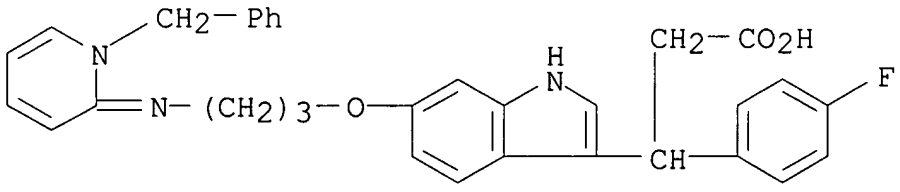
CRN 76-05-1
CMF C2 H F3 O2



RN 354822-82-5 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-(4-fluorophenyl)-6-[3-[[1-(phenylmethyl)-2(1H)-pyridinylidene]amino]propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

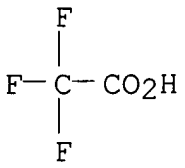
CRN 354822-81-4
CMF C32 H30 F N3 O3



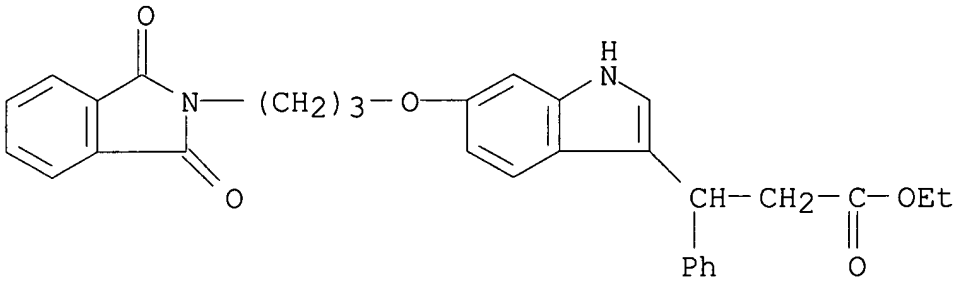
CM 2

CRN 76-05-1

CMF C2 H F3 O2



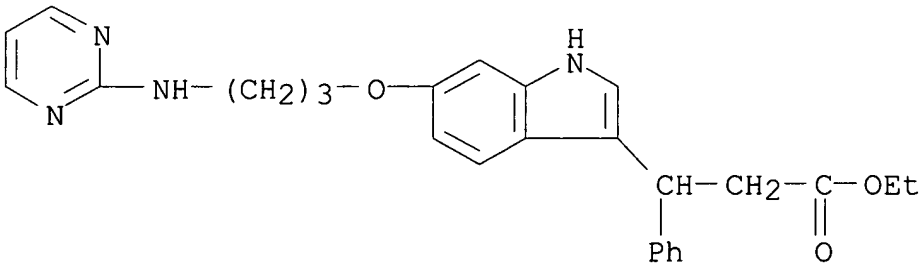
RN 354823-11-3 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)propoxy]-.beta.-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 354823-20-4 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-(2-pyrimidinylamino)propoxy]-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

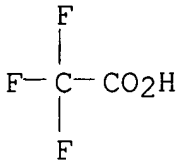
CM 1

CRN 354823-19-1
CMF C26 H28 N4 O3

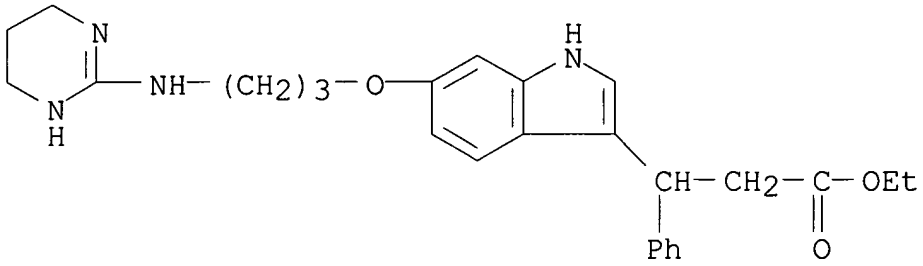


CM 2

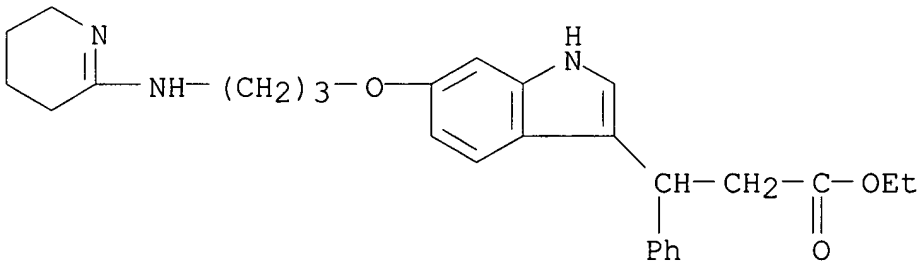
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-23-7 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



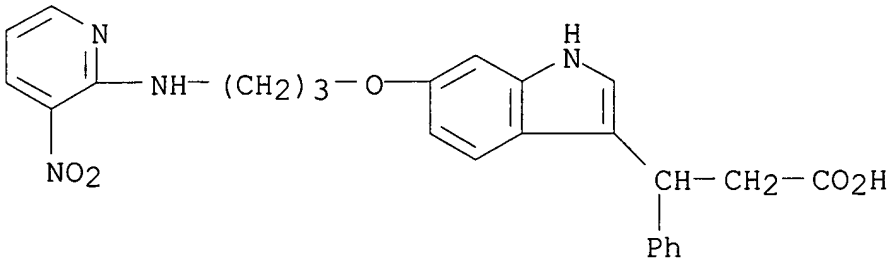
RN 354823-26-0 ZCA
CN 1H-Indole-3-propanoic acid, .beta.-phenyl-6-[3-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]propoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 354823-38-4 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(3-nitro-2-pyridinyl)amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

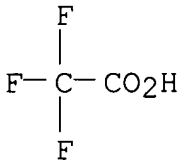
CM 1

CRN 354823-37-3
CMF C25 H24 N4 O5



CM 2

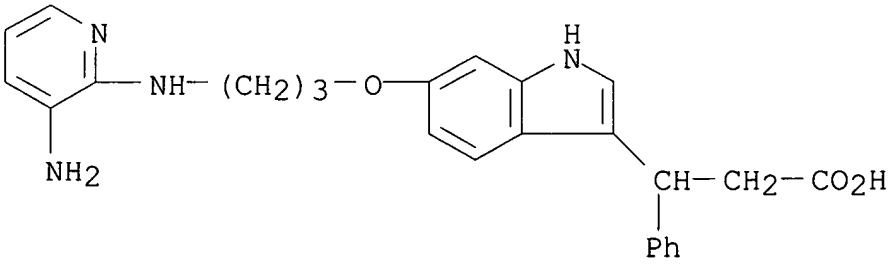
CRN 76-05-1
CMF C2 H F3 O2



RN 354823-40-8 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[(3-amino-2-pyridinyl)amino]propoxy]-.beta.-phenyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

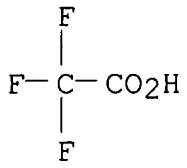
CRN 354823-39-5
CMF C25 H26 N4 O3



CM 2

CRN 76-05-1

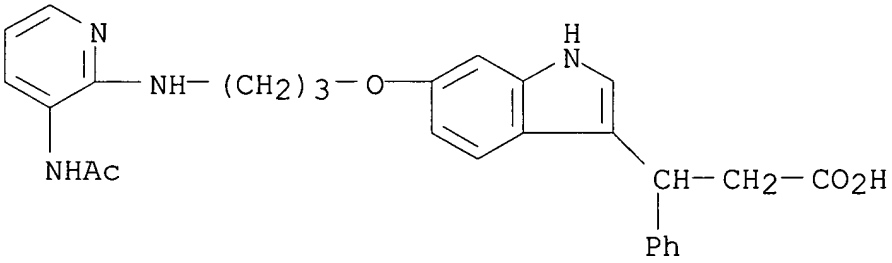
CMF C2 H F3 O2



RN 354823-43-1 ZCA
CN 1H-Indole-3-propanoic acid, 6-[3-[[3-(acetylamino)-2-pyridinyl]amino]propoxy]-.beta.-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

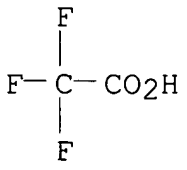
CM 1

CRN 354823-42-0
CMF C27 H28 N4 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2



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354823-56-6P 354823-71-5P
(prepn. of indolylpropionates as integrin inhibitors)

IT **354823-46-4P**
(prepn. of indolylpropionates as integrin inhibitors)

IT **354822-55-2P 354822-57-4P 354822-59-6P**
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354823-43-1P
(prepn. of indolylpropionates as integrin inhibitors)

L11 ANSWER 6 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 134:17503 ZCA
TITLE: Preparation of 5-[4-benzylpiperidinyl(piperazinyl)]-indolecarboxamides as inhibitors of p38 kinase
INVENTOR(S): Mavunkel, Babu J.; Chakravarty, Sarvajit; Perumattam, John J.; Dugar, Sundeep; Lu, Qing; Liang, Xi
PATENT ASSIGNEE(S): Scios Inc., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071535	A1	20001130	WO 2000-US14003 <--	200005 19

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SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
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OTHER SOURCE(S): MARPAT 134:17503
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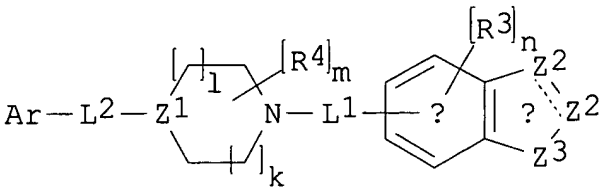

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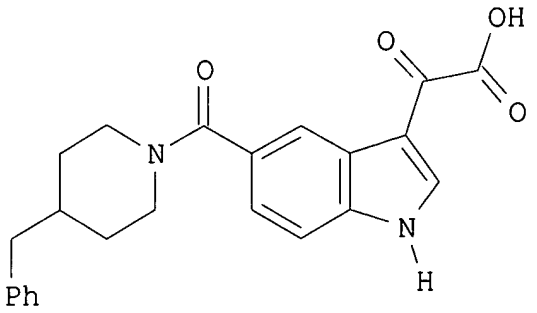


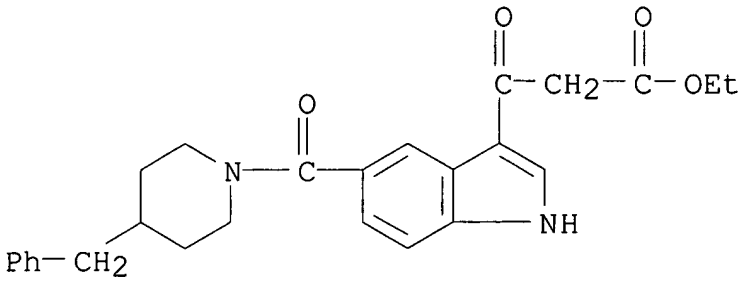
II

AB The title compds. [I; one Z2 = CA, CR8A and the other = CR1, CR12, NR6, N (wherein R1, R6, R8 = H, noninterfering substituent; A = WiCOXjY; Y = COR2, an isostere; R2 = H, noninterfering substituent; W, X = spacer of 2-6.ANG.; i, j = 0-1); Z3 = NR7, O; R3 = noninterfering substituent; n = 0-3; L1, L2 = linker; R4 = noninterfering substituent; m = 0-4; Z1 = CR5, N (R5 = H, noninterfering substituent); l, k = 0-2, wherein the sum of l and k = 0-3; Ar = aryl substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring; the distance between the atom of Ar linked to L2 and the center of the .alpha. ring is 4.5-24.ANG.] which inhibit p38-.alpha. kinase (biol. data given), were prepd. Thus, treating 6-methoxy-(4-benzylpiperidinyl)-indole-5-carboxamide with oxalyl chloride in CH2Cl2 afforded the indole-5-carboxamide II.

IT **309915-11-5P**
(prepn. of 5-[4-benzylpiperidinyl(piperazinyl)]-indolecarboxamides as inhibitors of p38 kinase)

RN 309915-11-5 ZCA

CN 1H-Indole-3-propanoic acid, .beta.-oxo-5-[[4-(phenylmethyl)-1-piperidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **309915-11-5P**
(prepn. of 5-[4-benzylpiperidinyl(piperazinyl)]-indolecarboxamides as inhibitors of p38 kinase)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 133:57509 ZCA
TITLE: Formation and characterization of a single Trp-Trp cross-link in indolicidin that confers protease stability without altering antimicrobial activity
AUTHOR(S): Osapay, Klara; Tran, Dat; Ladokhin, Alexey S.; White, Stephen H.; Henschen, Agnes H.; Selsted, Michael E.
CORPORATE SOURCE: Department of Pathology, University of California, Irvine, CA, 92697, USA
SOURCE: Journal of Biological Chemistry (**2000**), 275(16), 12017-12022
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indolicidin is a 13-residue cationic, antimicrobial peptide-amide isolated from the cytoplasmic granules of bovine neutrophils. The unique compn. of indolicidin distinguishes it from .alpha.-helical and .beta.-structured cationic peptides, because five of indolicidin's 13 residues are tryptophans: H-Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH2. Solid phase synthesis of indolicidin gave rise to a minor byproduct that possessed unusual fluorescence and UV absorbance properties compared with authentic indolicidin. The byproduct was purified by combined ion exchange and reversed phase high pressure liq. chromatog. steps and was shown be identical to authentic indolicidin in its microbicidal activity against Staphylococcus aureus, Escherichia coli, Candida albicans,

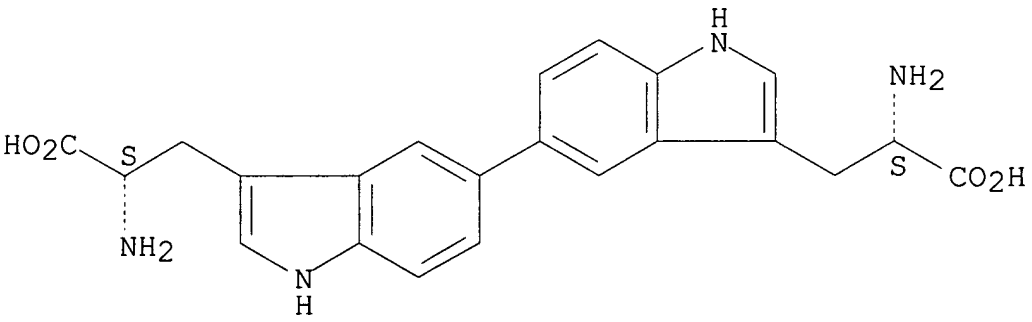
and Cryptococcus neoformans. Mass anal. of the byproduct revealed a 2-amu redn. compared with indolicidin, suggesting the deprotonation of two indole side chains to form an intrachain .delta.1,.delta.1'-ditryptophan deriv. The authors confirmed the nature of the cross-linked byproduct, termed X-indolicidin, by absorbance and fluorescence spectroscopy, peptide mapping, and sequence anal. Edman degrdn. revealed that Trp-6 and Trp-9 were covalently cross-linked. Compared with indolicidin, X-indolicidin was partially resistant to digestion with trypsin and chymotrypsin, suggesting that the ditryptophan stabilizes a subset of mol. conformations that are protease resistant but that are absent in the native structure.

IT **276681-45-9**, .delta.1,.delta.1'-Ditryptophan
(of indolicidin deriv. with protease stability and antimicrobial activity)

RN 276681-45-9 ZCA

CN [5,5'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-, (.alpha.S,.alpha.'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **276681-45-9**, .delta.1,.delta.1'-Ditryptophan
(of indolicidin deriv. with protease stability and antimicrobial activity)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 133:17316 ZCA

TITLE: Photochemical reactions of derivatives of pyrimidine bases

AUTHOR(S): Celewicz, Lech

CORPORATE SOURCE: Poznan, Pol.

SOURCE: Seria Chemia (Uniwersytet im. Adama Mickiewicza w Poznaniu) (**1999**), 67, 1-106
CODEN: SCUCDH; ISSN: 0554-8241

PUBLISHER: Wydawnictwo Naukowe Uniwersytetu im. Adama Mickiewicza w Poznaniu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish
OTHER SOURCE(S): CASREACT 133:17316

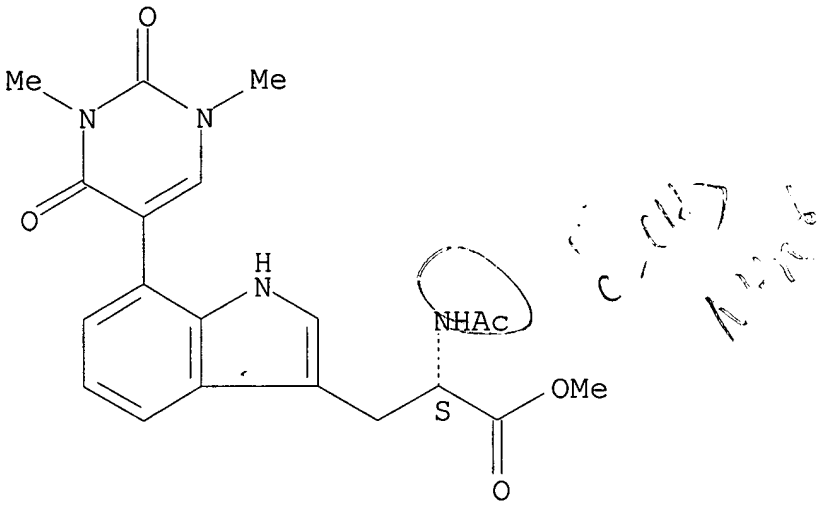
AB Photochem. reactions of some pyrimidine bases and their derivs. have been studied. Photoreactions of 5-methylcytosine and 5-methyl-2'-deoxycytidine with water lead to 3-amino-2-methylacrylamidine and 3-(2-deoxy-D-erythro-pentopyranos-1-yl)amino-2-methylacrylamidine, resp. Photoreaction of 5-fluorocytosine with methanol yields initially 5-fluoro-6-methoxy-5,6-dihydrocytosine which undergoes fast conversion to cytosine, 6-methoxycytosine and 5-methoxycytosine. Photoreaction of 5-bromo-1,3-dimethyluracil with N.alpha.-acetyl-L-tryptophan Me ester yields not only N.alpha.-acetyl-2-(uracil-5-yl)-L-tryptophan Me ester but also N.alpha.-acetyl-7-(uracil-5-yl)-L-tryptophan Me ester. Photoreactions of 5-bromocytosine, 5-bromo-1-methylcytosine and 5-bromo-2'-deoxycytidine with N.alpha.-acetyl-L-tryptophan N-ethylamide lead to N.alpha.-acetyl-2-(cytosin-5-yl)-L-tryptophan N-ethylamide, N.alpha.-acetyl-2-(1-methylcytosin-5-yl)-L-tryptophan N-ethylamide and N.alpha.-acetyl-2-[1-(2-deoxy-.beta.-D-erythro-pentofuranosyl)cytosin-5-yl]-L-tryptophan N-ethylamide, resp. 5-Fluorouracil and 5-fluoro-2'-deoxyuridine undergo photoreactions with N.alpha.-acetyl-L-tryptophan N-ethylamide yielding N.alpha.-acetyl-2-(uracil-5-yl)-L-tryptophan N-ethylamide and N.alpha.-acetyl-2-[1-(2-deoxy-.beta.-D-erythro-pentofuranosyl)uracil-5-yl]-L-tryptophan N-ethylamide, resp. These data are preceded by a review of 165 refs.

IT **123739-87-7P**
(photochem. reactions of derivs. of pyrimidine bases)

RN 123739-87-7 ZCA

CN L-Tryptophan, N-acetyl-7-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-5-pyrimidinyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **123739-87-7P**
(photochem. reactions of derivs. of pyrimidine bases)

L11 ANSWER 9 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 132:237222 ZCA
TITLE: Preparation of polyacetate-derived phorboids anti-inflammatory and other pharmaceutical uses
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 68 pp., Cont.-in-part of U.S. Ser. No. 349,128.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6043270	A	20000328	US 1995-480160	19950607
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JP 09221450	A2	19970826	JP 1996-318803	19870610
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US 5643948	A	19970701	US 1993-120643	19930909

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US 5962498	A	19991005	US 1994-349128	
				199412
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JP 08268961	A2	19961015	JP 1996-69274	
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PRIORITY APPLN. INFO.:			US 1986-872812	B2
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JP 1987-503773 A3
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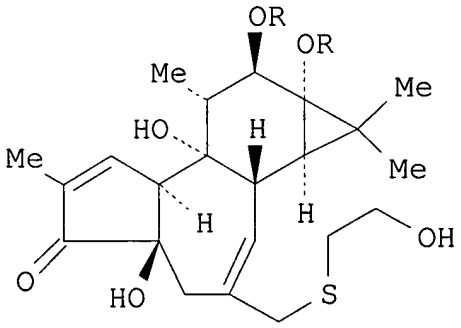
OTHER SOURCE(S): MARPAT 132:237222

GI



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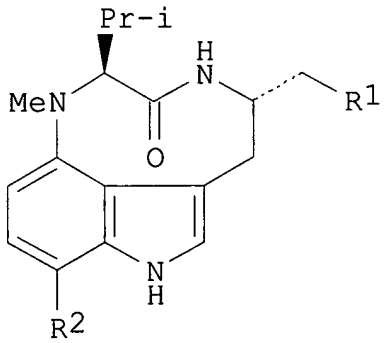


II

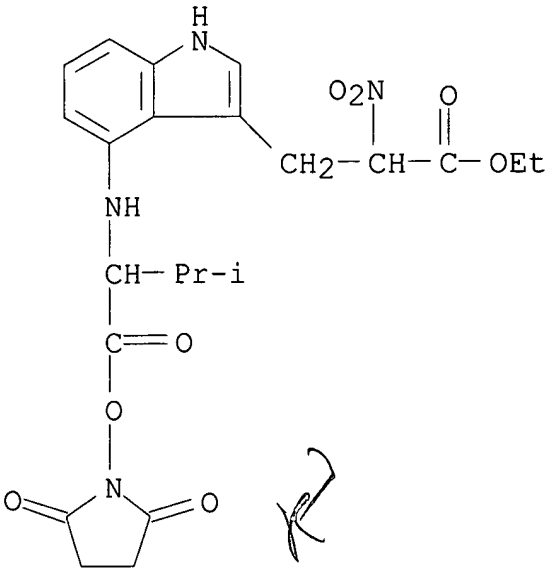
AB Benzolactams and phorboids P-G (P = a radical derived from a phorbol diterpene or indole lactam; G = group of .ltoreq. 55 atoms) were prepd. as protein kinase C modulators with anti-inflammatory, anti-viral, anti-melanoma, anti-leukemia, and other activities for pharmaceutical use. Thus, phorbol deriv. I [R = CO(CH2)2Me] and indolactam V deriv. II [R1 = OP(S)(OMe)2, R2 = octyl] were prepd. starting from 20-deoxy-20-chlorophorbol 12,13-dibutyrate and (-)-7-octylindolactam V, resp. The prepd. compds. were tested for anti-HIV, anti-melanoma, anti-leukemia, and antitumor activities.

IT **160255-53-8P**
(prepn. of polyacetate-derived phorboids having anti-inflammatory and other pharmaceutical uses)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-,

ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of polyacetate-derived phorboids having anti-inflammatory and other pharmaceutical uses)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 132:3304 ZCA
Correction of: 131:184851
TITLE: Fluorination of 3-(3-(Piperidin-1-yl)propyl)indoles and 3-(3-(1-piperazinyl)propyl)indoles gives selective human 5-HT1D receptor ligands with improved pharmacokinetic profiles
AUTHOR(S): van Niel, Monique B.; Collins, Ian; Beer, Margaret S.; Broughton, Howard B.; Cheng, Susan K. F.; Goodacre, Simon C.; Heald, Anne; Locker, Karen L.; MacLeod, Angus M.; Morrison, Denise; Moyes, Christopher R.; O'Connor, Desmond; Pike, Andrew; Rowley, Michael; Russel, N.; Sohal, Balbinder; Stanton, Josephine A.; Thomas, Steven; Verrier, Hugh; Watt, Alan P.; Castro, Jose L.
CORPORATE SOURCE: Department of Medicinal Chemistry Department of Biochemistry and Drug Metabolism and Pharmacokinetics Group Merck, Sharp Dohme

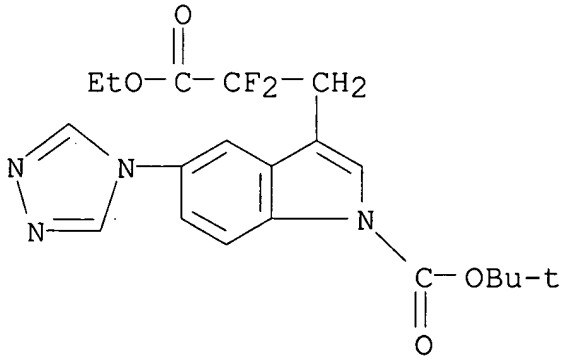
Research Laboratories, Harlow, CM20 2QR, UK
SOURCE: Journal of Medicinal Chemistry (**1999**), 42(12), 2087-2104
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has previously been reported that a 3-(3-(1-piperazinyl)propyl)indole series of 5-HT1D receptor ligands have pharmacokinetic advantages over the corresponding 3-(3-(piperidin-1-yl)propyl)indole series and that the reduced pKa of the piperazines compared to the piperidines may be one possible explanation for these differences. To investigate this proposal, versatile synthetic strategies for the incorporation of fluorine into these ligands, producing novel series of 4-fluoropiperidines, 3-fluoro-4-aminopiperidines, and both piperazine and piperidine derivs. with one or two fluorines in the Pr linker were developed. Ligands were identified which maintained high affinity and selectivity for the 5-HT1D receptor and showed agonist efficacy in vitro. The incorporation of fluorine was found to significantly reduce the pKa of the compds., and this redn. of basicity was shown to have a dramatic, beneficial influence on oral absorption, although the effect on oral bioavailability could not always be accurately predicted.

IT **191212-91-6P**
(prepn. and activity of fluorinated [(piperidinyl)propyl](triazolyl)indoles or [(pyridazinyl)propyl](triazolyl)indoles as human 5-HT1D receptor ligands)

RN 191212-91-6 ZCA

CN 1H-Indole-3-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-.alpha.,.alpha.-difluoro-5-(4H-1,2,4-triazol-4-yl)-, ethyl ester (9CI) (CA INDEX NAME)



IT **191212-91-6P**
(prepn. and activity of fluorinated [(piperidinyl)propyl](triazol

yl)indoles or [(pyridazinyl)propyl](triazolyl)indoles as human 5-HT1D receptor ligands)

L11 ANSWER 11 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 131:337208 ZCA
TITLE: Preparation of phorboid derivatives as protein kinase C modulators
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 75 pp., Cont.-in-part of U.S. 5,643,948.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5955501	A	19990921	US 1995-480191	19950607
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JP 09221450	A2	19970826	JP 1996-318803	19870610
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US 5145842	A	19920908	US 1990-559701	19900730
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US 5643948	A	19970701	US 1993-120643	19930913
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JP 08268961	A2	19961015	JP 1996-69274	19960228
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WO 9640614	A1	19961219	WO 1996-US9710	19960607
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W: JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1986-872812 B2 19860606

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US	1987-61299	B2	198706 10
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US	1989-322881	A2	198903 13
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US	1993-120643	A2	199309 13
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US	1993-120643	A2	199309 13
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JP	1987-503773	A3	198706

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US 1992-980907 A2 199211 24
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US 1995-472871 A 199506 07
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US 1995-480191 A 199506 07
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US 1995-480251 A 199506 07
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OTHER SOURCE(S): MARPAT 131:337208

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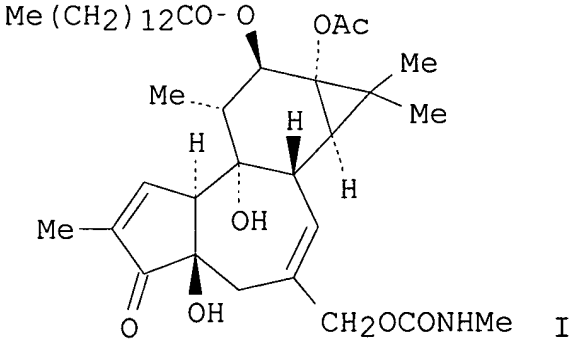
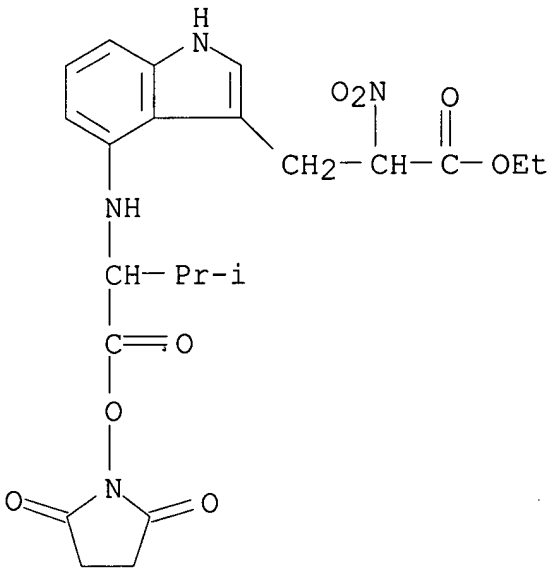


I

AB Compds. derived from phorboids of the diterpene- and benzolactam-classes are prepd. with anti-inflammatory and other activities. Thus, I is prepd. from phorbol 12-myristate-13-acetate and Me isocyanate. I showed antileukemic activity against HL-60 cells (IC50 = 2.6 .mu.M). Pharmaceutical compns. contg. the title compds. are described.

IT **160255-53-8P**
(prepn. of phorboid derivs. with anti-inflammatory and other activities)

RN 160255-53-8 ZCA
CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of phorboid derivs. with anti-inflammatory and other activities)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 131:184851 ZCA
TITLE: Fluorination of 3-(3-(Piperidin-1-yl)propyl)indoles and 3-(3-(1-piperazinyl)propyl)indoles Gives Selective Human 5-HT1D Receptor Ligands with Improved Pharmacokinetic Profiles
AUTHOR(S): Van Niel, Monique B.; Collins, Ian; Beer, Margaret S.; Broughton, Howard B.; Cheng, Susan K. F.; Goodacre, Simon C.; Heald, Anne; Locker, Karen L.; MacLeod, Angus M.; Morrison, Denise; Moyes, Christopher R.; O'Connor, Desmond; Pike, Andrew; Rowley, Michael; Russell, Michael G. N.; Sohal, Balbinder; Stanton, Josephine A.; Thomas, Steven; Verrier, Hugh; Watt, Alan P.; Castro, Jose L.
CORPORATE SOURCE: Department of Medicinal Chemistry Department of

Biochemistry and Drug Metabolism and Pharmacokinetics Group Merck, Sharp Dohme Research Laboratories, Harlow Essex, CM20 2QR, UK

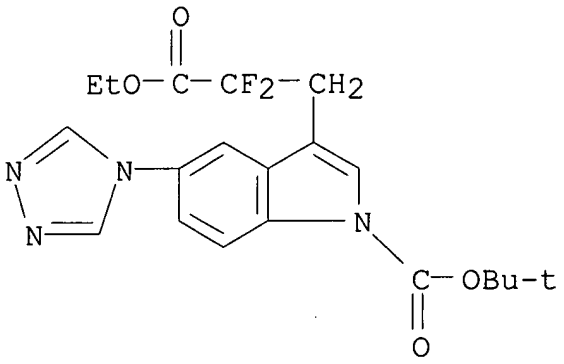
SOURCE: Journal of Medicinal Chemistry (**1999**), 42(12), 2087-2104
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:184851

AB It has previously been reported that a 3-(3-(1-piperazinyl)propyl)indole series of 5-HT1D receptor ligands have pharmacokinetic advantages over the corresponding 3-(3-(piperidin-1-yl)propyl)indole series and that the reduced pKa of the piperazines compared to the piperidines may be one possible explanation for these differences. To investigate this proposal, versatile synthetic strategies for the incorporation of fluorine into these ligands, producing novel series of 4-fluoropiperidines, 3-fluoro-4-aminopiperidines, and both piperazine and piperidine derivs. with one or two fluorines in the Pr linker were developed. Ligands were identified which maintained high affinity and selectivity for the 5-HT1D receptor and showed agonist efficacy in vitro. The incorporation of fluorine was found to significantly reduce the pKa of the compds., and this redn. of basicity was shown to have a dramatic, beneficial influence on oral absorption, although the effect on oral bioavailability could not always be accurately predicted.

IT **191212-91-6P**
(prepn. and activity of fluorinated [(piperidinyl)propyl](triazolyl)indoles or [(pyridazinyl)propyl](triazolyl)indoles as human 5-HT1D receptor ligands)

RN 191212-91-6 ZCA

CN 1H-Indole-3-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-.alpha.,.alpha.-difluoro-5-(4H-1,2,4-triazol-4-yl)-, ethyl ester (9CI) (CA INDEX NAME)



IT **191212-91-6P**
(prepn. and activity of fluorinated [(piperidinyl)propyl](triazol yl)indoles or [(pyridazinyl)propyl](triazolyl)indoles as human 5-HT1D receptor ligands)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 131:31874 ZCA
TITLE: Preparation of amidinophenylpropionylindoles and related compounds as thrombin inhibitors.
INVENTOR(S): Heckel, Armin; Walter, Rainer; Soyka, Rainer; Stassen, Jean-Marie; Wienen, Wolfgang; Binder, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928297	A1	19990610	WO 1998-EP7661 <--	19981127

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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19753522 A1 19990610 DE 1997-19753522 199712 03 <--

AU 9922671 A1 19990616 AU 1999-22671 199811 27 <--

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OTHER SOURCE(S): MARPAT 131:31874

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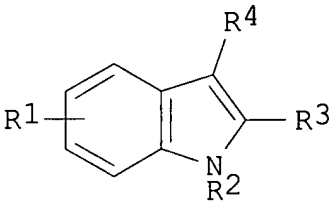
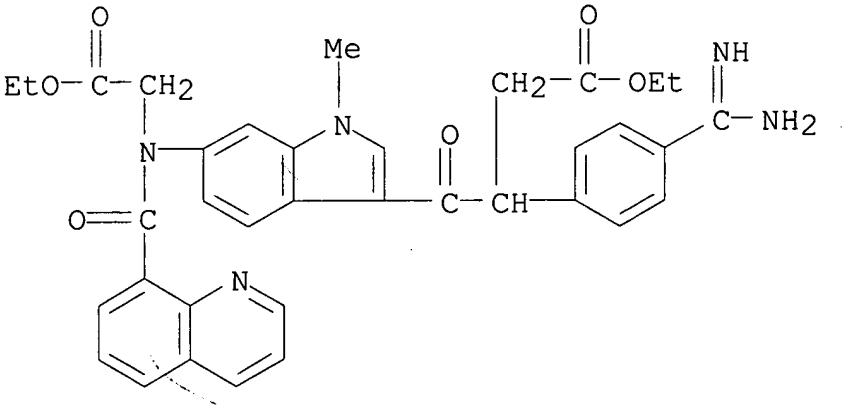


I

AB Title compds. [I; R1 = F, Cl, Br, CO2H, aminocarbonyl, aminosulfonyl, amino, group convertible to CO2H in vivo; 1 of R2, R4 = (CO2H- or group convertible to CO2H in vivo-substituted) alkyl, the other = R5A; A = (CO2H- or group convertible to CO2H in vivo-substituted) alkylene, etc.; R5 = R6NHC(:NH)-substituted Ph; R4 = H, alkyl; R6 = H, in vivo-cleavable group], were prepd. as antithrombotics with inhibitory activity against serine proteases XII and fibrinogen receptors. Thus, 3-[3-(4-amidinophenyl)propionyl]-1-methylindole-5-carboxylic acid N-(2-carboxyethyl)-N-phenylamide hydrochloride (prepn. given) showed a thrombin time ED200 = 0.80 .mu.M.

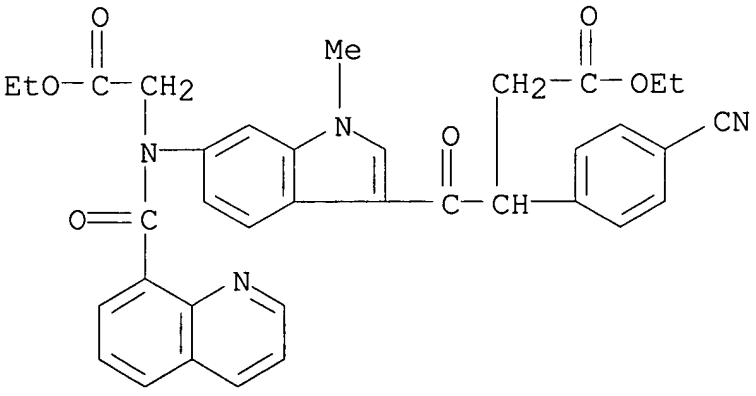
IT **226900-15-8P**
(prepn. of amidinophenylpropionylindoles and related compds. as thrombin inhibitors)

RN 226900-15-8 ZCA
CN 1H-Indole-3-butanoic acid, .beta.-[4-(aminoiminomethyl)phenyl]-6-[(2-ethoxy-2-oxoethyl)(8-quinolinylcarbonyl)amino]-1-methyl-.gamma.-oxo-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **226901-45-7P**
(prepn. of amidinophenylpropionylindoles and related compds. as thrombin inhibitors)
RN 226901-45-7 ZCA
CN 1H-Indole-3-butanoic acid, .beta.-(4-cyanophenyl)-6-[(2-ethoxy-2-oxoethyl)(8-quinolinylcarbonyl)amino]-1-methyl-.gamma.-oxo-, ethyl ester (9CI) (CA INDEX NAME)



IT **226900-15-8P**
(prepn. of amidinophenylpropionylindoles and related compds. as thrombin inhibitors)

IT **226901-45-7P**
(prepn. of amidinophenylpropionylindoles and related compds. as thrombin inhibitors)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:282199 ZCA
TITLE: Preparation of polyacetate-derived phorboids having anti-inflammatory and other pharmaceutical uses
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 67 pp., Cont.-in-part of U.S. Ser. No. 343,207.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891906	A	19990406	US 1995-472436 <--	19950607
JP 09221450	A2	19970826	JP 1996-318803 <--	19870610
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US 1992-980907 A2
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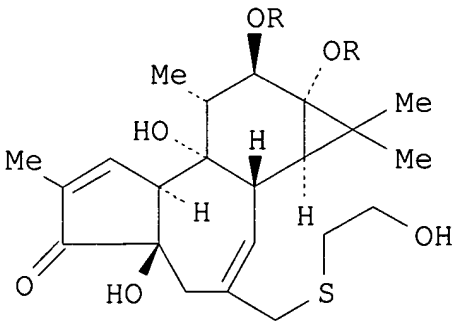
OTHER SOURCE(S): MARPAT 130:282199
GI



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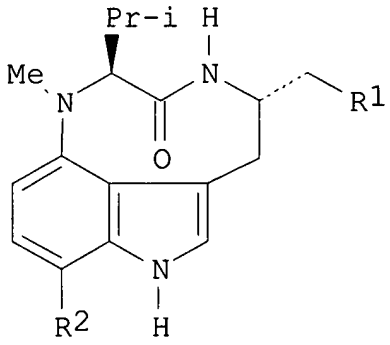


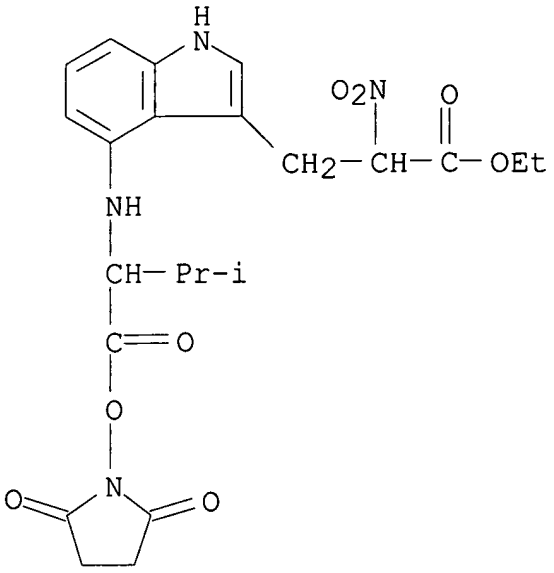
II

AB Benzolactams and phorboids P-G (P = a radical derived from a phorbol diterpene or indole lactam; G = group of .ltoreq. 55 atoms) were prepd. as protein kinase C modulators with anti-inflammatory, anti-viral, anti-melanoma, anti-leukemia, and other activities for pharmaceutical use. Thus, phorbol deriv. I [R = CO(CH2)2Me] and indolactam V deriv. II [R1 = OP(S)(OMe)2, R2 = octyl] were prepd. starting from 20-deoxy-20-chlorophorbol 12,13-dibutyrate and (-)-7-octylindolactam V, resp. The prepd. compds. were tested for anti-HIV, anti-melanoma, anti-leukemia, and antitumor activities.

IT **160255-53-8P**
(prepn. of polyacetate-derived phorboids having anti-inflammatory and other pharmaceutical uses)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of polyacetate-derived phorboids having anti-inflammatory and other pharmaceutical uses)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:282198 ZCA
TITLE: Preparation of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 70 pp., Cont.-in-part of U.S. Ser. No. 664,396.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891870	A	19990406	US 1995-472871	19950607

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JP 09221450	A2	19970826	JP 1996-318803	198706 10
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US 5145842	A	19920908	US 1990-559701	199007 30
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US 5643948	A	19970701	US 1993-120643	199309 13
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JP 08268961	A2	19961015	JP 1996-69274	199602 28
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WO 9640614	A1	19961219	WO 1996-US9710	199606 07
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W: JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:	US 1986-872812	B2	198606 11
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	US 1987-61299	B2	198706 10
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	US 1987-61299	YY	198706 10
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	US 1989-322851	B2	198903 13
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	US 1989-322881	B3	198903 13
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	US 1990-537885	B2	199006 14
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US 1990-559296	B2	19900730
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US 1990-559701	A2	19900730
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US 1991-664396	A2	19910304
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US 1991-664397	B2	19910304
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US 1993-120643	A2	19930913
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JP 1987-503773	A3	19870610
<--		
US 1992-980907	A2	19921124
<--		
US 1995-472871	A	19950607
<--		
US 1995-472890	A	19950607
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US 1995-480191	A	19950607
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US 1995-480251	A	19950607
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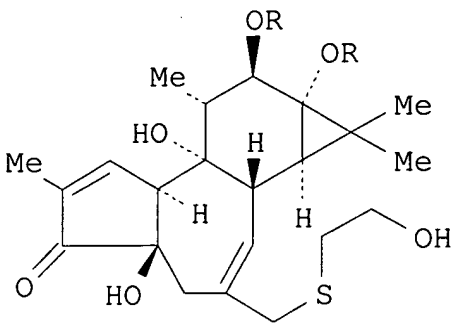
OTHER SOURCE(S): MARPAT 130:282198
GI



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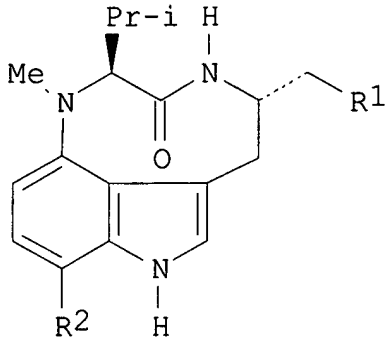


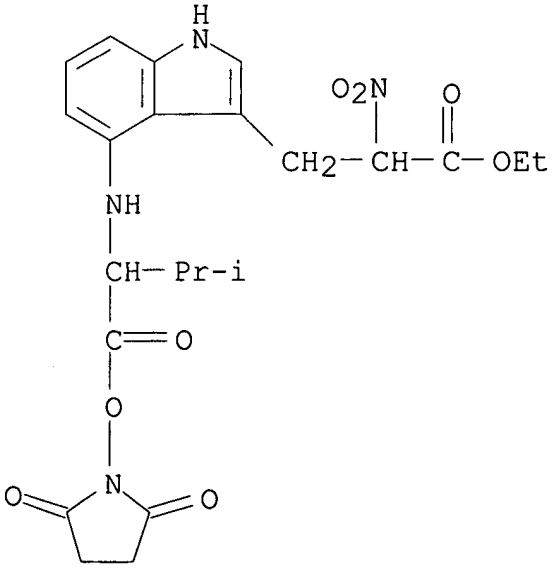
II

AB Benzolactams and phorboids P-G (P = a radical derived from a phorbol diterpene or indole lactam; G = group of .ltoreq. 55 atoms) were prepd. as protein kinase C modulators with anti-inflammatory, anti-viral, anti-melanoma, anti-leukemia, and other activities for pharmaceutical use. Thus, phorbol deriv. I [R = CO(CH2)2Me] and indolactam V deriv. II [R1 = OCONHMe, R2 = octyl] were prepd. starting from 20-deoxy-20-chlorophorbol 12,13-dibutyrate and (-)-7-octylindolactam V resp. The prepd. compds. were tested for anti-HIV, anti-melanoma, anti-leukemia, and antitumor activities.

IT **160255-53-8P**
(prepn. of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:252508 ZCA
TITLE: Preparation of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 940,440.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886019	A	19990323	US 1995-475522 <--	19950607
JP 09221450	A2	19970826	JP 1996-318803 <--	19870610
US 5145842	A	19920908	US 1990-559701 <--	19900730
US 5886017	A	19990323	US 1992-940440 <--	19920904
US 5643948	A	19970701	US 1993-120643 <--	19930913
JP 08268961	A2	19961015	JP 1996-69274	19960

28

PRIORITY APPLN. INFO.:	US 1986-872812 <--	B2	198606 11
	US 1987-61299 <--	B3	198706 10
	US 1989-322881 <--	B2	198903 13
	US 1990-559701 <--	A2	199007 30
	US 1991-664397 <--	B2	199103 04
	US 1992-940440 <--	A2	199209 04
	US 1993-120643 <--	A2	199309 13
	JP 1987-503773 <--	A3	198706 10
	US 1990-537885 <--	B2	199006 14
	US 1990-559296 <--	B2	199007 30
	US 1992-980907 <--	A2	199211 24

OTHER SOURCE(S): MARPAT 130:252508
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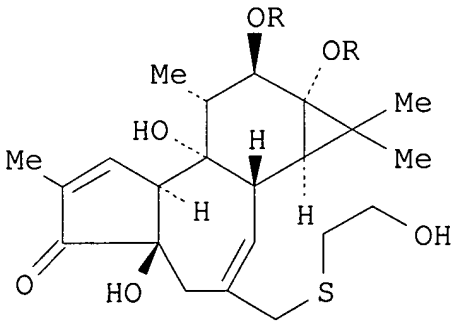

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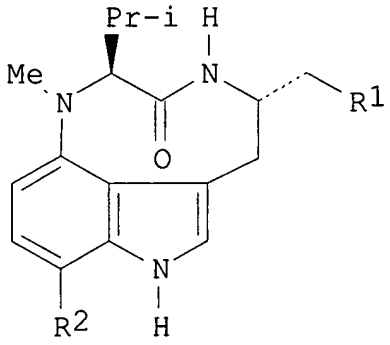


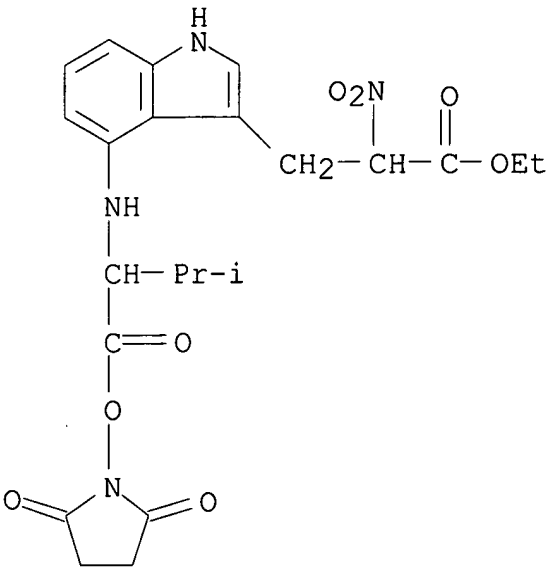
II

AB Benzolactams and phorboids P-G (P = a radical derived from a phorbol diterpene or indole lactam; G = group of .ltoreq. 55 atoms) were prepd. as protein kinase C modulators with anti-inflammatory, anti-viral, anti-melanoma, anti-leukemia, and other activities for pharmaceutical use. Thus, phorbol deriv. I [R = CO(CH2)2Me] and indolactam V deriv. II [R1 = OP(O)(OMe)N(CHMe2)2, R2 = octyl] were prepd. starting from 20-deoxy-20-chlorophorbol 12,13-dibutyrate and (-)-7-octylindolactam V resp. The prepd. compds. were tested for anti-HIV, anti-melanoma, anti-leukemia, and antitumor activities.

IT **160255-53-8P**
(prepn. of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of phorbol diterpenes and indolactams as protein kinase C modulators for pharmaceutical use)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:252507 ZCA
TITLE: Preparation of phorbol and indolactam derivs. for pharmaceutical use as protein kinase C modulators
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 38 pp., Cont.-in-part of U.S. 5,145,842.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886017	A	19990323	US 1992-940440	19920904

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JP 09221450	A2	19970826	JP 1996-318803	19870610
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US 5145842	A	19920908	US 1990-559701	19900730
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US 5886019	A	19990323	US 1995-475522	19950607
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JP 08268961	A2	19961015	JP 1996-69274	19960228
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PRIORITY APPLN. INFO.:

US 1986-872812	B2	19860611
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US 1987-61299	B3	19870610
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US 1989-322881	B2	19890313
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US 1990-559701	A2	19900730
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JP 1987-503773	A3	19870610
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US 1991-664397	B2	19910304
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US 1992-940440	A2	19920904
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US 1993-120643	A2	19930913
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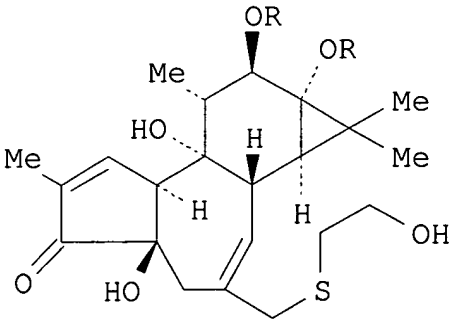
OTHER SOURCE(S): MARPAT 130:252507
GI



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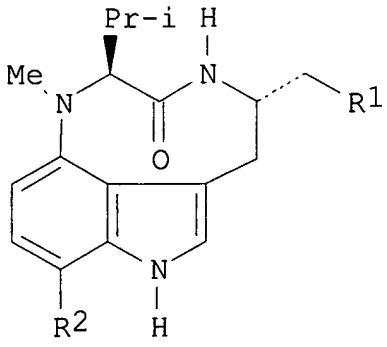


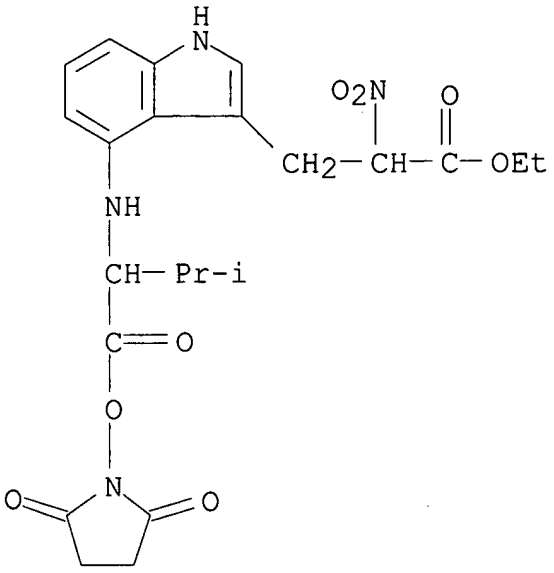
II

AB Benzolactams and phorboids P-G (P = a radical derived from a phorbol diterpene or indole lactam; G = group of .ltoreq. 55 atoms selected from C, H, O, etc.) were prepd. as protein kinase C modulators with anti-inflammatory, anti-viral and other activities for pharmaceutical use. Thus, phorbol deriv. I [R = CO(CH2)2Me] and indolactam V deriv. II (R1 = OCONHMe, R2 = octyl) were prepd. starting from 20-deoxy-20-chlorophorbol 12,13-dibutyrate and (-)-7-octylindolactam V resp. The prepd. compds. were tested for anti-HIV activity.

IT **160255-53-8P**
(prepn. of phorbol and indolactam derivs. for pharmaceutical use as protein kinase C modulators)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of phorbol and indolactam derivs. for pharmaceutical use as protein kinase C modulators)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

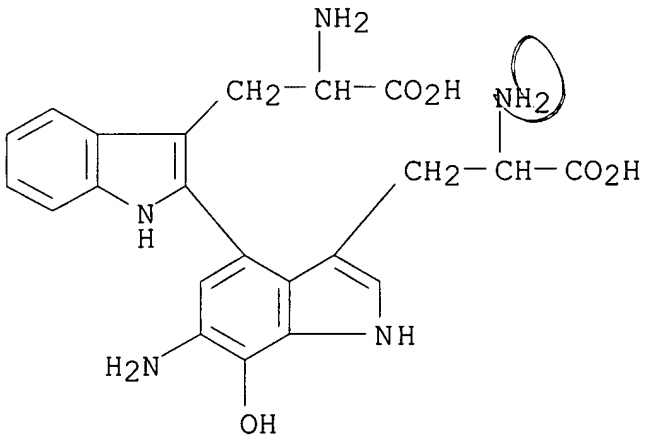
L11 ANSWER 18 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 130:22163 ZCA
TITLE: Crystallographic and spectroscopic studies of native, aminoquinol, and monovalent cation-bound forms of methylamine dehydrogenase from Methylobacterium extorquens AM1
AUTHOR(S): Labesse, Gilles; Ferrari, Davide; Chen, Zhi-Wei; Rossi, Gian-Luigi; Kuusk, Vladisav; McIntire, William S.; Mathews, F. Scott
CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Journal of Biological Chemistry (**1998**), 273(40), 25703-25712
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Various monovalent cations influence the enzymic activity and the spectroscopic properties of methylamine dehydrogenase (MADH). Here,

we report the structure detn. of this tryptophan tryptophylquinone-contg. enzyme from Methylobacterium extorquens AM1 by high resoln. x-ray crystallog. (1.75 .ANG.). This first MADH crystal structure at low ionic strength is compared with the high resoln. structure of the related MADH from Paracoccus denitrificans recently reported. We also describe the first structures (at 1.95 to 2.15 .ANG. resoln.) of an MADH in the substrate-reduced form and in the presence of trimethylamine and of cesium, two competitive inhibitors. Polarized absorption microspectrophotometry was performed on single crystals under various redox, pH, and salt conditions. The results show that the enzyme is catalytically active in the crystal and that the cations cause the same spectral perturbations as are obsd. in soln. These studies lead us to propose a model for the entrance and binding of the substrate in the active site.

IT **178115-33-8**
(crystallog. and spectroscopic studies of native, aminoquinol, and monovalent cation-bound forms of methylamine dehydrogenase from Methylobacterium extorquens AM1)

RN 178115-33-8 ZCA

CN [2,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.',6'-triamino-7'-hydroxy- (9CI) (CA INDEX NAME)



IT **178115-33-8**
(crystallog. and spectroscopic studies of native, aminoquinol, and monovalent cation-bound forms of methylamine dehydrogenase from Methylobacterium extorquens AM1)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 129:28105 ZCA

TITLE: Preparation of diterpene phorboids and indolactams as protein kinase C modulators for pharmaceutical use

INVENTOR(S): Driedger, Paul E.; Quick, James

PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA

SOURCE: U.S., 61 pp., Cont.-in-part of U.S. Ser. No. 120,643.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 13

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5750568	A	19980512	US 1995-480699 <--	19950607
JP 09221450	A2	19970826	JP 1996-318803 <--	19870610
US 5145842	A	19920908	US 1990-559701 <--	19900730
US 5643948	A	19970701	US 1993-120643 <--	19930913
JP 08268961	A2	19961015	JP 1996-69274 <--	19960228

PRIORITY APPLN. INFO.:

US 1986-872812 <--	B2	19860611
US 1987-61299 <--	B2	19870610
US 1989-322881 <--	YY	19890313

US 1989-322881 B2 198903 13
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US 1990-537885 B2 199006 14
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US 1990-559296 B2 199007 30
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US 1990-559701 A2 199007 30
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US 1991-664397 B2 199103 04
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US 1992-980907 B2 199211 24
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US 1993-120643 A2 199309 13
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JP 1987-503773 A3 198706 10
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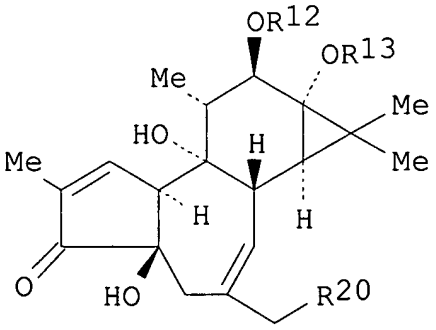
OTHER SOURCE(S): MARPAT 129:28105
GI



I

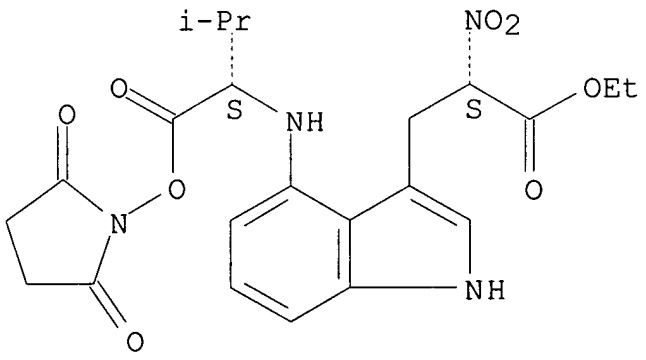
AB Diterpene phorboids, such as I [R12 = R13 = H, acyl; R20 = H, OH, SH, NH2, halo, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, ureido, substituted amino, etc.], as well as indolactam alkaloids, were prepd. and formulated for a variety of pharmaceutical uses, such as antiviral, antiinflammatory, antileukemia, and antitumor agents. Thus, I [R12 = myristoyl, R13 = acetyl, R20 = SCH2CH2OH] was prepd. via condensation of I [R12 = myristoyl, R13 = acetyl, R20 = Cl] with HSCH2CH2OH using 2,4,6-collidine in MeCN, and showed antimelanoma activity when tested against human RPMI-7272 melanoma cells.

IT **208034-41-7P 208034-45-1P**
(prepn. of diterpene phorboids and indolactams as protein kinase C modulators for pharmaceutical use)

RN 208034-41-7 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[(1R)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester, (.alpha.R)-rel- (9CI) (CA INDEX NAME)

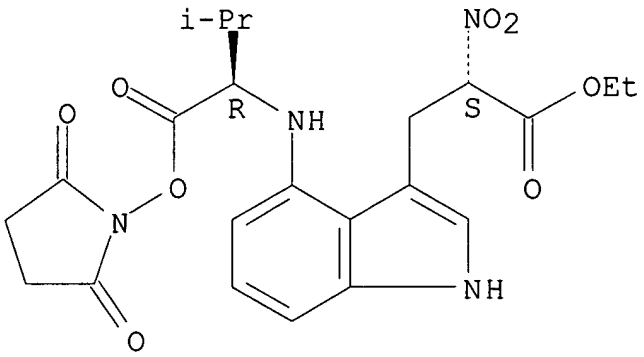
Relative stereochemistry.



RN 208034-45-1 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[(1R)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester, (.alpha.S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **208034-41-7P 208034-45-1P**
(prepn. of diterpene phorboids and indolactams as protein kinase C modulators for pharmaceutical use)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 128:167580 ZCA
TITLE: Preparation of phorboids as protein kinase C modulators
INVENTOR(S): Driedger, Paul E.; Quick, James
PATENT ASSIGNEE(S): Procyon Pharmaceuticals, Inc., USA
SOURCE: U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 343,207.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5716968	A	19980210	US 1995-476702 <--	19950607
JP 09221450	A2	19970826	JP 1996-318803 <--	19870610
US 5643948	A	19970701	US 1993-120643	19930913

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JP 08268961	A2	19961015	JP 1996-69274		19960228
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PRIORITY APPLN. INFO.:			US 1986-872812	B2	19860611
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			US 1987-61299	B2	19870610
			<--		
			US 1989-322881	B3	19890313
			<--		
			US 1990-559296	B2	19900730
			<--		
			US 1991-664396	B2	19910304
			<--		
			US 1992-980906	B1	19921124
			<--		
			US 1993-120643	A2	19930913
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			US 1994-343207	A2	19941122
			<--		
			JP 1987-503773	A3	19870610
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			US 1990-537885	B2	19900614
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			US 1990-559701	A2	19900730

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US 1991-664397 A2 19910304
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US 1992-980907 A2 19921124
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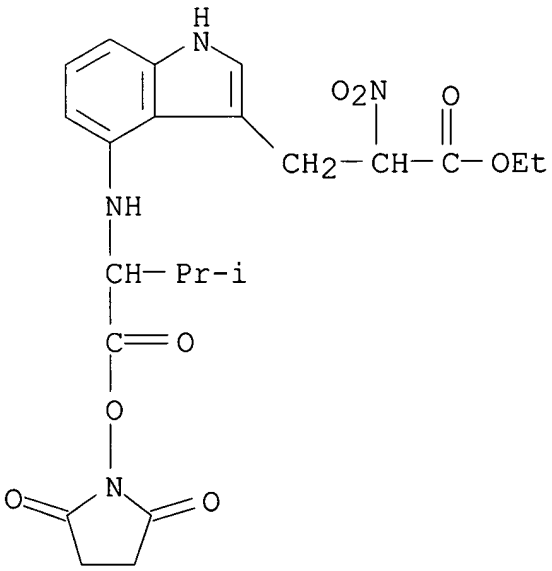
OTHER SOURCE(S): MARPAT 128:167580

AB Compns. having anti-inflammatory, antiviral and other activities are prepd. The compns. are derived from phorboids of the diaminobenzyl alc.- and diacylglycerol-classes. Thus, dibromotriphenylphosphorane was added to phorbol 12,13-bis(2,4-difluorophenylacetate) to form 20-deoxy-20-bromophorbol 12,13-bis(2,4-difluorophenylacetate) (I). The anti-HIV ED50 value for RNA of I was less than 1 nM.

IT **160255-53-8P**
(prepn. of phorboids as protein kinase C modulators)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(prepn. of phorboids as protein kinase C modulators)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 127:65786 ZCA
TITLE: Piperazine, piperidine and tetrahydropyridine derivatives useful as selective 5-HT agonists
INVENTOR(S): Castro Pineiro, Jose Luis; Macleod, Angus Murray; Rowley, Michael; Van Niel, Monique Bodil
PATENT ASSIGNEE(S): Merck Sharp and Dohme Limited, UK
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718203	A1	19970522	WO 1996-GB2762	19961113
			<--	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2236294	AA	19970522	CA 1996-2236294	19961113
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AU 9675782	A1	19970605	AU 1996-75782	19961113
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AU 712059	B2	19991028		
EP 863895	A1	19980916	EP 1996-938319	19961113
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 5977116	A	19991102	US 1998-68680	19980512
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PRIORITY APPLN. INFO.: GB 1995-23250 A 199511 14
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WO 1996-GB2762 W 199611 13
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OTHER SOURCE(S): MARPAT 127:65786

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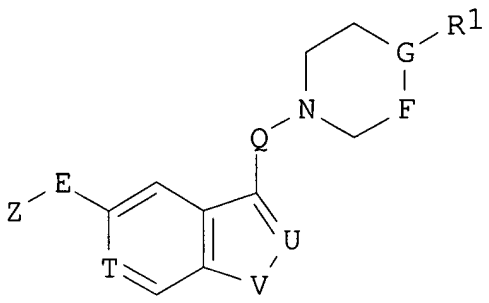

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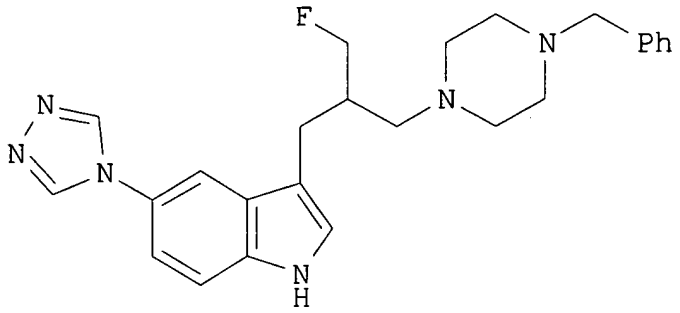


II

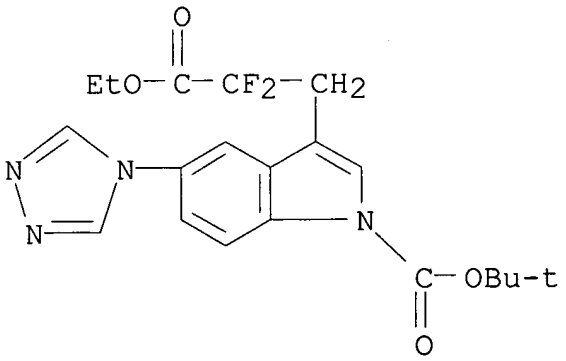
AB A class of N-substituted piperazine, piperidine, and tetrahydropyridine derivs. is claimed, specifically I [Z = H, halo, cyano, NO2, CF3, (un)substituted OH, CO2H, or NH2, certain (un)substituted 5-membered heteroaryls, etc.; E = bond, alkylene; Q = (fluoro)alkylene; T = N, CH; U = N, CR2; V = O, S, NR3; FG = CH2N, CH2CH, CH:C; R1 = (un)substituted alkenyl, alkynyl, (hetero)aralkyl; R2, R3 = H, alkyl] and their salts and prodrugs. The compds. are selective agonists of 5-HT1-like receptors, being potent agonists of the human 5-HT1D.alpha. receptor subtype while possessing at least a 10-fold selective affinity for that receptor subtype relative to the

5-HT1D.beta. subtype. I are therefore useful for treatment of migraine and assocd. disorders, while eliciting fewer side-effects (esp. adverse cardiovascular events) than do non-subtype-selective 5-HT1D receptor agonists. For instance, cyclization of the acetal 4-benzyl-1-[4-(1,3-dioxolan-2-yl)-2-(hydroxymethyl)butyl]piperazine with 4-(1,2,4-triazol-4-yl)phenylhydrazine gave an indole deriv., which underwent mesylation at the hydroxymethyl group, and subsequent reaction of the mesylate with Bu4N+ F-, to give title compd. II. In a 5-HT1D.alpha./5-HT1D.beta. adenylyl cyclase assay, all tested I showed EC50 values below 500 nM at 5-HT1D.alpha. receptors, and at least 10-fold selectivity as described above.

IT **191212-91-6P**
(intermediate; prepn. of piperazine, piperidine and tetrahydropyridine derivs. as selective 5-HT agonists)

RN 191212-91-6 ZCA

CN 1H-Indole-3-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-.alpha.,.alpha.-difluoro-5-(4H-1,2,4-triazol-4-yl)-, ethyl ester (9CI) (CA INDEX NAME)



IT **191212-91-6P**
(intermediate; prepn. of piperazine, piperidine and tetrahydropyridine derivs. as selective 5-HT agonists)

L11 ANSWER 22 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 127:50649 ZCA

TITLE: Preparation of heterocyclyl-substituted azetidine, pyrrolidine and piperidine derivatives as selective agonists of 5-HT1-like receptors

INVENTOR(S): Castro Pineiro, Jose Luis; MacLeod, Angus Murray; Van Niel, Monique Bodil

PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718201	A1	19970522	WO 1996-GB2764	19961113
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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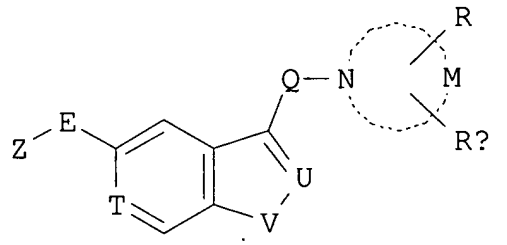
AU 9675784	A1	19970605	AU 1996-75784	19961113
			<--	
AU 711546	B2	19991014		
EP 861244	A1	19980902	EP 1996-938321	19961113
			<--	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 5998440	A	19991207	US 1998-68620	19980508
			<--	
PRIORITY APPLN. INFO.:			GB 1995-23243 A	19951114
			<--	
			WO 1996-GB2764 W	19961113
			<--	

OTHER SOURCE(S): MARPAT 127:50649
GI



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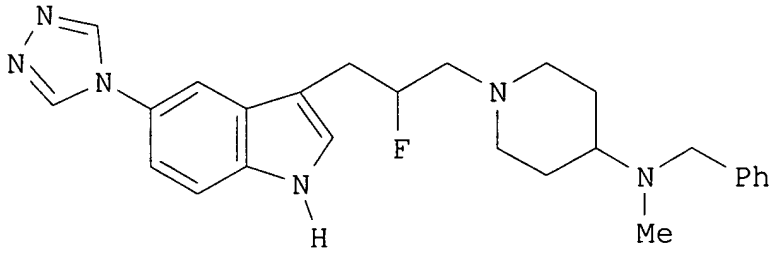


II

AB The title compds. [I; Z = H, halo, CN, etc.; E = a chem. bond, C1-4 alkylene; Q = C1-6 alkylene (substituted in any position by one or more F atoms), T = N, CH; U = N, CH, C(C1-6 alkyl); V = O, S, NH, N(C1-6 alkyl); M = the residue of an azetidine, pyrrolidine, piperidine; R = WR1 (wherein W = a chem. bond, C1-4 alkylene; R1 = OH, SH, NH2, etc.); Ra = H, OH, alkyl, heterocyclyl], selective agonists of 5-HT1-like receptors, being potent agonists of the human 5-HT1D.alpha. receptor subtype while possessing at least a 10-fold selective affinity for the 5-HT1D.alpha. receptor subtype relative to the 5-HT1D.beta. subtype and therefore useful in the treatment and/or prevention of clin. conditions, in particular migraine and assocd. disorders, for which a subtype-selective agonist of 5-HT1D receptors is indicated, while eliciting fewer side-effects, notably adverse cardiovascular events, than those assocd. with non-subtype-selective 5-HT1D receptor agonists, were prepd. Thus, treatment of (R,S)-2-fluoro-3-[5-(1,2,4-triazol-4-yl)-1H-indol-3-yl]propan-1-ol with MeSO2Cl in the presence of Et3N in THF followed by reaction of the mesylate with 4-(N-benzyl-N-methylamino)piperidine in the presence of K2CO3 in iPrOH afforded 55% II which showed IC50 of < 50 nM against binding to the 5-HT1D.alpha. receptor subtype. Compds. I are effective in the treatment of migraine at 0.05-5 mg/kg/day.

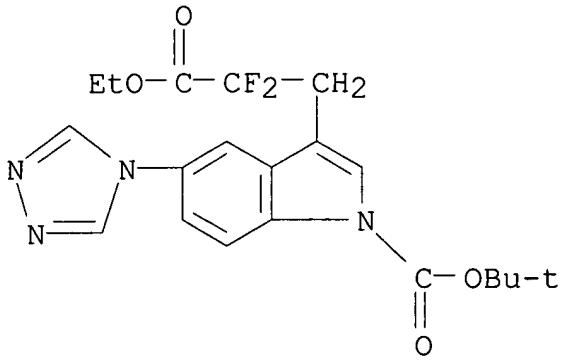
IT **191212-91-6P**

(prepn. of heterocyclyl-substituted azetidine, pyrrolidine and

piperidine derivs. as selective agonists of 5-HT1-like receptors)

RN 191212-91-6 ZCA

CN 1H-Indole-3-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-.alpha.,.alpha.-difluoro-5-(4H-1,2,4-triazol-4-yl)-, ethyl ester (9CI) (CA INDEX NAME)



IT **191212-91-6P**

(prepn. of heterocyclyl-substituted azetidine, pyrrolidine and piperidine derivs. as selective agonists of 5-HT1-like receptors)

L11 ANSWER 23 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 126:56713 ZCA

TITLE: Direct Detection by 15N NMR of the Tryptophan Tryptophylquinone Aminoquinol Reaction Intermediate of Methylamine Dehydrogenase

AUTHOR(S): Bishop, G. Reid; Valente, Edward J.; Whitehead, Tracy L.; Brown, Kenneth L.; Hicks, Rickey P.; Davidson, Victor L.

CORPORATE SOURCE: Medical Center, University of Mississippi, Jackson, MS, 39216-4505, USA

SOURCE: Journal of the American Chemical Society (**1996**), 118(50), 12868-12869
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

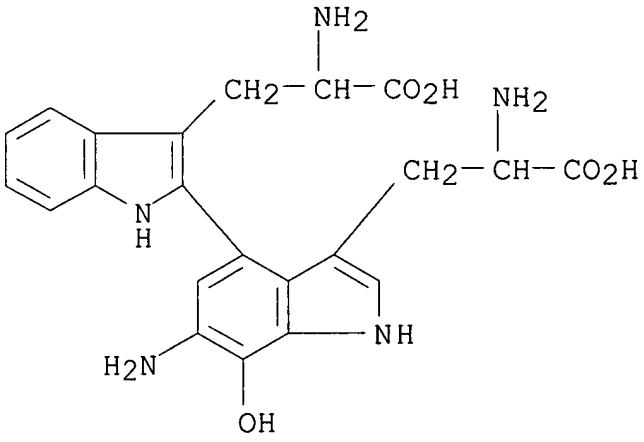
AB Data from 15N-NMR expts. are presented which directly confirm the existence of the aminoquinol form of the amino-acid derived tryptophan tryptophylquinone (TTQ) cofactor of methylamine dehydrogenase (MADH) from Paracoccus denitrificans. We demonstrate that redn. of MADH by excess 15N enriched methylammonium chloride results in the formation of two discrete N signals. The first, positioned at .delta. = 35, accumulates maximally with long pulse delay (60 s) and is attributable to free unreacted methylammonium ion; the second appears at .psi. = 54 ppm optimally with short pulse

delay (1.0 s). The relaxation time and chem. shift of the new N species at .delta. = 54 are fully consistent with 15N covalently bound to an arom. ring (i.e., aminoquinol) which is attached to a rigid protein matrix. Exhaustive dialysis results in loss of the alkylammonium signal at .delta. = 35 ppm and retention of the arom. aminoquinol signal at .delta. = 54 ppm. Oxidn. of the reduced enzyme results in liberation of the arom. N signal (.delta. = 54) as free ammonium ion (.delta. = 35). These results confirm: (i) the existence of a stable covalent aminoquinol TTQ intermediate formed during the physiol. redn. of MADH by substrate methylamine, (ii) the instability of oxidized iminoquinone TTQ and release of ammonium only after reoxidn. of MADH, and (iii) the value of 15N-NMR in monitoring the fate of substrate-derived N during the catalytic cycles of enzymes, such as MADH, which catalyze the transformation of biol. amines.

IT **178115-33-8**
(direct detection by 15N NMR of the tryptophan tryptophylquinone cofactor aminoquinol reaction intermediate of Paracoccus denitrificans methylamine dehydrogenase)

RN 178115-33-8 ZCA

CN [2,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.',6'-triamino-7'-hydroxy- (9CI) (CA INDEX NAME)



IT **178115-33-8**
(direct detection by 15N NMR of the tryptophan tryptophylquinone cofactor aminoquinol reaction intermediate of Paracoccus denitrificans methylamine dehydrogenase)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 125:52127 ZCA

TITLE: Evidence for a Tryptophan Tryptophylquinone Aminosemiquinone Intermediate in the Physiologic Reaction between Methylamine Dehydrogenase and Amicyanin

AUTHOR(S): Bishop, G. Reid; Brooks, Harold B.; Davidson, Victor L.

CORPORATE SOURCE: Medical Center, University of Mississippi, Jackson, MS, 39216-4505, USA

SOURCE: Biochemistry (**1996**), 35(27), 8948-8954
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

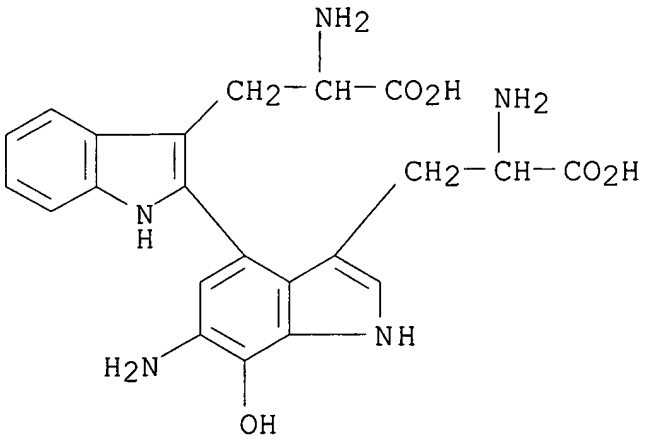
LANGUAGE: English

AB The tryptophan tryptophylquinone (TTQ) cofactor of methylamine dehydrogenase (MADH) is covalently modified by nitrogen during its two-electron redn. by methylamine to form an aminoquinol (N-quinol). It is possible, in vitro, to generate unmodified O-quinol and O-semiquinone forms of MADH with dithionite, as well as an N-semiquinone form which contains a substrate-derived nitrogen. Rapid-scanning stopped-flow spectroscopy and global kinetic anal. are used to demonstrate that N-semiquinone is a true physiol. reaction intermediate which accumulates during the two sequential one-electron oxidns. of N-quinol MADH by amicyanin. In contrast, no detectable O-semiquinone accumulates during the two sequential one-electron oxidns. of the O-quinol form of MADH by amicyanin. This is because the reaction of N-semiquinone with amicyanin is much slower (70 s-1 at 25.degree.) than the reaction of O-semiquinone (>1000 s-1). These rate consts. obtained from global anal. of the overall reaction are the same as those obtained when each semiquinone form was made in vitro and then mixed with oxidized amicyanin. The presence of 200 mM NH4Cl during the reaction of O-quinol MADH with amicyanin does not cause any detectable accumulation of a semiquinone species. Thus, the accumulation of the intermediate in the reactions of the N-quinol is not due to the influence of noncovalently bound ammonia at the active site of the O-semiquinone. These data indicate that the intermediate which accumulates during the complete oxidn. of substrate-reduced N-quinol MADH is not the O-semiquinone, but the more slowly reacting N-semiquinone, and that the N-semiquinone is a physiol. relevant reaction intermediate. These results also provide good evidence in favor of an aminotransferase mechanism, as opposed to an imine elimination mechanism, for the reaction of MADH with substrate methylamine.

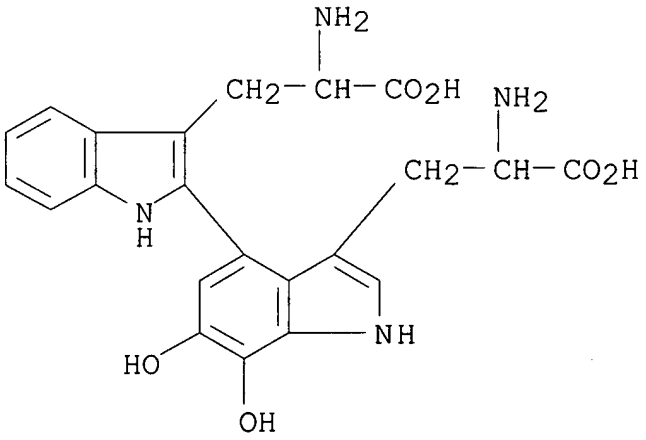
IT **178115-33-8 178115-35-0**
(evidence for a tryptophan tryptophylquinone aminosemiquinone intermediate in physiol. oxidn. of methylamine dehydrogenase by amicyanin)

RN 178115-33-8 ZCA

CN [2,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.',6'-triamino-7'-hydroxy- (9CI) (CA INDEX NAME)



RN 178115-35-0 ZCA
CN [2,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-6',7'-dihydroxy- (9CI) (CA INDEX NAME)



IT **178115-33-8 178115-35-0**
(evidence for a tryptophan tryptophylquinone aminosemiquinone intermediate in physiol. oxidn. of methylamine dehydrogenase by amicyanin)

L11 ANSWER 25 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 124:30306 ZCA
TITLE: Oxidation chemistry of 5-[[3-(2-amino-2-carboxyethyl)-5-hydroxy-1H-indol-4-yl]oxy]-3-(2-amino-2-carboxyethyl)-1H-indole: a putative aberrant metabolite of 5-hydroxytryptophan

AUTHOR(S): Wu, Zheng; Shen, Xue-Ming; Dryhurst, Glenn
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. Oklahoma, Norman, OK, 73019, USA
SOURCE: Bioorganic Chemistry (**1995**), 23(3), 227-55
CODEN: BOCMBM; ISSN: 0045-2068
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oxidative damage is known to occur in certain regions of the brain in a no. of neurodegenerative disorders that include Alzheimer's Disease (AD) and transient cerebral ischemia and as a result of methamphetamine abuse. Furthermore, aberrant but unknown oxidized forms of 5-hydroxytryptophan (5-HTPP) and 5-hydroxytryptamine (5-HT) have been detected in the cerebrospinal fluid (CSF) of AD patients but not in that of age-matched controls. Accordingly, it is possible that aberrant oxidative metabolites of 5-HTPP and 5-HT might play roles in the neurodegenerative processes that occur in the AD brain and other neurodegenerative disorders. Previous studies have established that the title compd. (1) is among the products of the electrochem. driven and various enzyme-mediated oxidns. of 5-HTPP. This investigation has focused on both the electrochem. and peroxidase-mediated oxidns. of 1 at physiol. pH and has established that this dimer is significantly more easily oxidized than 5-HTPP from which it is derived. Under weakly oxidizing conditions 1 is oxidized via a putative carbocation intermediate to an equimolar mixt. of 5-HTPP and tryptophan-4,5-dione (2). Under more strongly oxidizing conditions further oxidn. of 5-HTPP gives a C(4)-centered carbocation intermediate that can react with the free hydroxyl residue of 1 to form a trimer, tetramer, and larger oligomers that are subsequently further oxidized ultimately to dione 2. When administered into the brains of mice, 1 is a remarkably lethal compd. (LD50 = 3.3 .mu.g) and evokes a hyperactivity syndrome. Analyses of the brains of mice during this behavioral response reveal that an acute dose of 1 evokes a significant decrease of norepinephrine (NE) levels. Only minor alterations in whole brain levels of dopamine (DA) and 5-HT occur but levels of 3,4-dihydroxyphenylacetic acid, homovanillic acid, and 5-hydroxyindole-3-acetic acid are significantly elevated. These results suggest that the hyperactivity syndrome evoked by 1 is related to the elevated release and turnover of NE, DA and 5-HT. Based upon the results obtained and by comparison with other pharmacol. manipulations that evoke a similar hyperactivity syndrome in mice and rats, it appears that 1 might be metabolized in vivo to metabolites that interact with certain 5-HT and perhaps other receptor subpopulations.

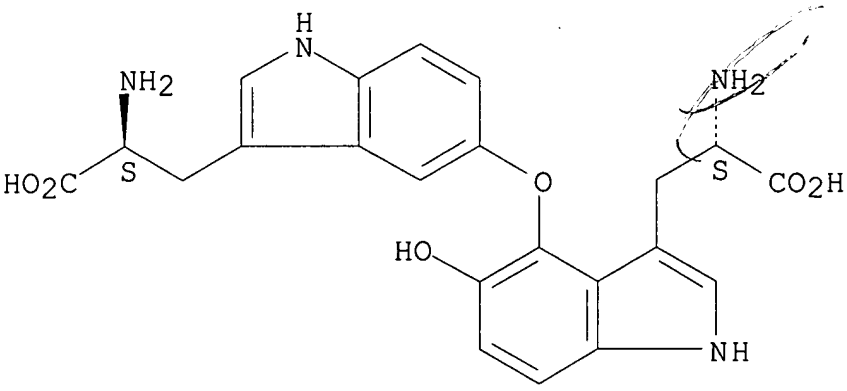
IT **147502-85-0P**
(prepn. and oxidn. chem. of [[(aminocarboxyethyl)hydroxyindolyl]o

xy](aminocarboxyethyl)indole, putative aberrant metabolite of hydroxytryptophan)

RN 147502-85-0 ZCA

CN L-Tryptophan, 4-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-5-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

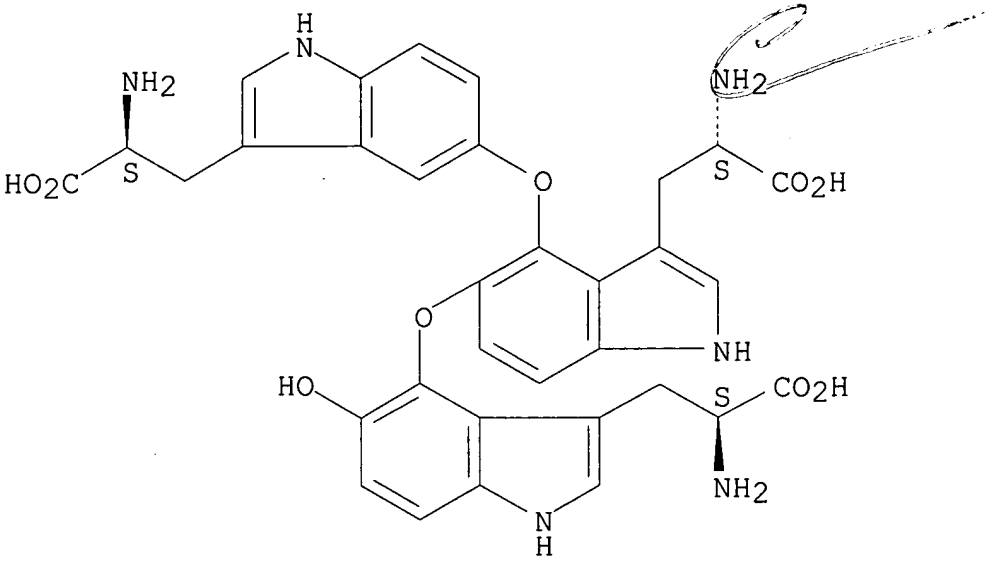


IT **171776-51-5P 171776-52-6P 171776-53-7P**
(prepn. and oxidn. chem. of [[(aminocarboxyethyl)hydroxyindolyl]oxy](aminocarboxyethyl)indole, putative aberrant metabolite of hydroxytryptophan)

RN 171776-51-5 ZCA

CN L-Tryptophan, 5-[[3-(2-amino-2-carboxyethyl)-5-hydroxy-1H-indol-4-yl]oxy]-4-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

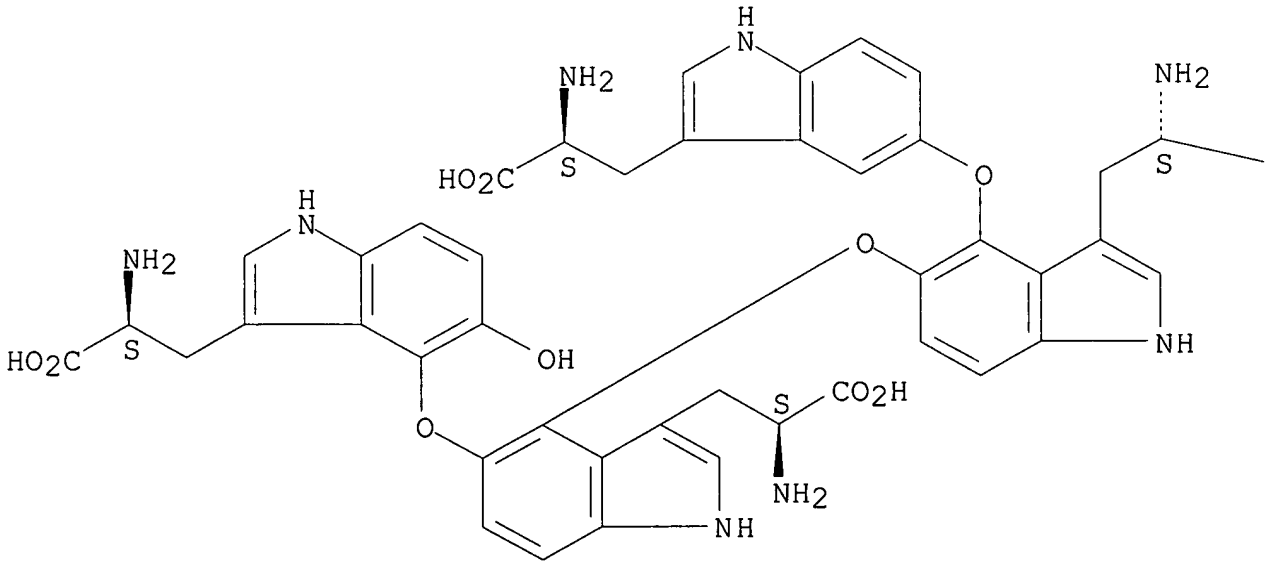
Absolute stereochemistry.



RN 171776-52-6 ZCA
CN L-Tryptophan, 5-[[3-(2-amino-2-carboxyethyl)-5-[[3-(2-amino-2-carboxyethyl)-5-hydroxy-1H-indol-4-yl]oxy]-1H-indol-4-yl]oxy]-4-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-, stereoisomer (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



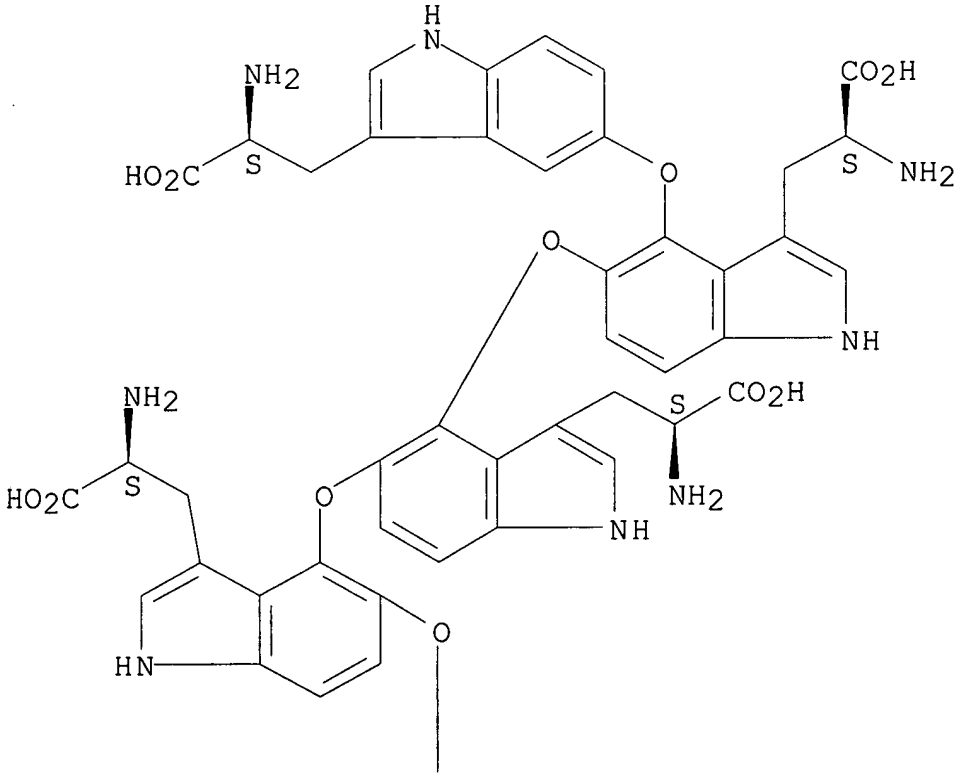
PAGE 1-B

—CO_2H

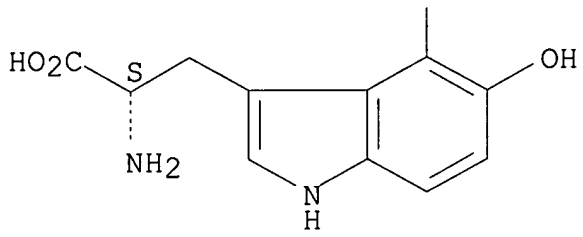
RN 171776-53-7 ZCA
CN L-Tryptophan, 5-[[3-(2-amino-2-carboxyethyl)-5-[[3-(2-amino-2-carboxyethyl)-5-hydroxy-1H-indol-4-yl]oxy]-1H-indol-4-yl]oxy]-4-[[3-(2-amino-2-carboxyethyl)-4-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-1H-indol-5-yl]oxy]-, stereoisomer (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



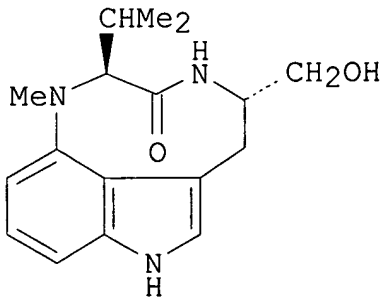
PAGE 2-A



IT **147502-85-0P**
(prepn. and oxidn. chem. of [[(aminocarboxyethyl)hydroxyindolyl]oxy](aminocarboxyethyl)indole, putative aberrant metabolite of hydroxytryptophan)

IT **171776-51-5P 171776-52-6P 171776-53-7P**
(prepn. and oxidn. chem. of [[(aminocarboxyethyl)hydroxyindolyl]oxy](aminocarboxyethyl)indole, putative aberrant metabolite of hydroxytryptophan)

L11 ANSWER 26 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 122:81719 ZCA
TITLE: Protein kinase C modulators. Indolactams. 1. Efficient and flexible routes for the preparation of (-)-Indolactam V for use in the synthesis of analogs
AUTHOR(S): Quick, James; Saha, Bijali; Driedger, Paul E.
CORPORATE SOURCE: Procyon Pharmaceuticals, Inc., Woburn, MA, 01801, USA
SOURCE: Tetrahedron Letters (**1994**), 35(46), 8549-52
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:81719
GI



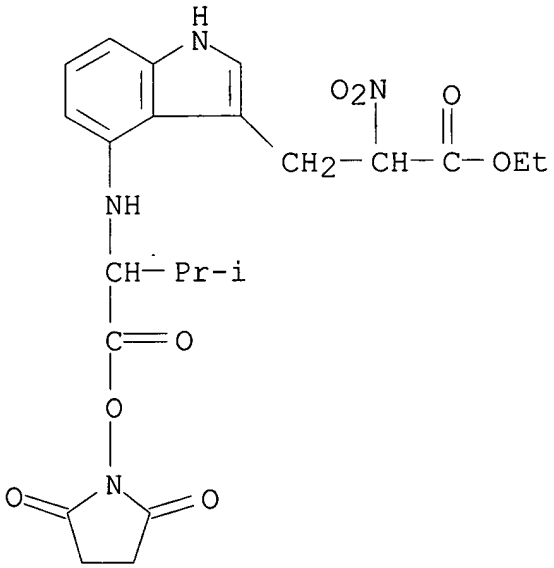
I

AB Three syntheses of the protein kinase C activator, (-)-indolactam V (ILV, I), are described and are compared for their potential utility in the prepn. of ILV analogs. In one route the 4-amino functionality is introduced regiospecifically during the construction of the indole portion and enantiomeric control is achieved by the alkylation of the amine with a triflate derived from D-valine. One of the routes affords racemic ILV from which (-)-ILV is obtained by the first reported resoln. of an indolactam.

IT **160255-53-8P**
(efficient and flexible routes for the prepn. of indolactam V for use in the synthesis of analogs)

RN 160255-53-8 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, ethyl ester (9CI) (CA INDEX NAME)



IT **160255-53-8P**
(efficient and flexible routes for the prepn. of indolactam V for use in the synthesis of analogs)

L11 ANSWER 27 OF 35 ZCA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 118:243252 ZCA

TITLE: Electrochemical and enzymic oxidation of 5-hydroxytryptophan

AUTHOR(S): Humphries, Keith A.; Wrona, Monika Z.; Dryhurst, Glenn

CORPORATE SOURCE: Dep. Chem. Biochem., Univ. Oklahoma, Norman, OK,

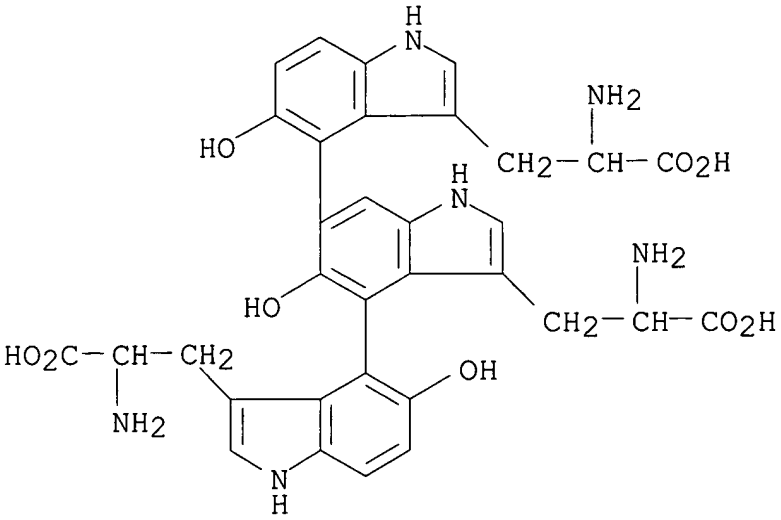
73019, USA
SOURCE: Journal of Electroanalytical Chemistry (**1993**), 346(1-2), 377-403
CODEN: JECHES; ISSN: 0368-1874
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L-5-Hydroxytryptophan (5-HTPP) is the immediate precursor of the neurotransmitter 5-hydroxytryptamine (5-HT) in the central nervous system. Aberrant but unknown oxidized forms of 5-HTPP and 5-HT were detected in the cerebrospinal fluid (CSF) of patients with Alzheimer's disease. To provide some clues to the identities of the unknown oxidized forms of 5-HTPP in Alzheimer CSF, the electrochem. driven and enzyme-mediated (peroxidase + H2O2, ceruloplasmin + O2, tyrosinase + O2) oxidns. of this indole were studied. The key intermediate in these oxidn. reactions, which appear to proceed by very similar chem. pathways, is a C4-centered carbocation (2b) which reacts with available nucleophiles. Reaction of 2b with H2O ultimately leads to tryptophan-4,5-dione. Reaction of 2b with 5-HTPP (an ion-substrate dimerization) gives diastereomers of 5,5'-dihydroxy-4,4'-bi-tryptophan (A and B) and a further dimer (J) linked at the space group C4 position of one 5-HTPP residue and the C5-O position of the other. Carbocation 2b also attacks dimers A, B and J to give a family of trimeric compds. Methods for the isolation of reaction products are described, and spectral information supporting the proposed structures is given.

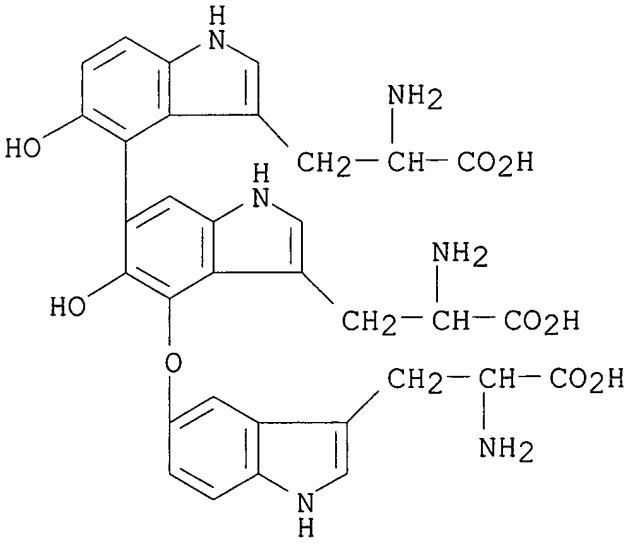
IT **129738-78-9 147502-87-2 147502-89-4**
(cyclic voltammetry of, electrochem. and enzymic oxidn. of hydroxytryptophan in relation to)

RN 129738-78-9 ZCA

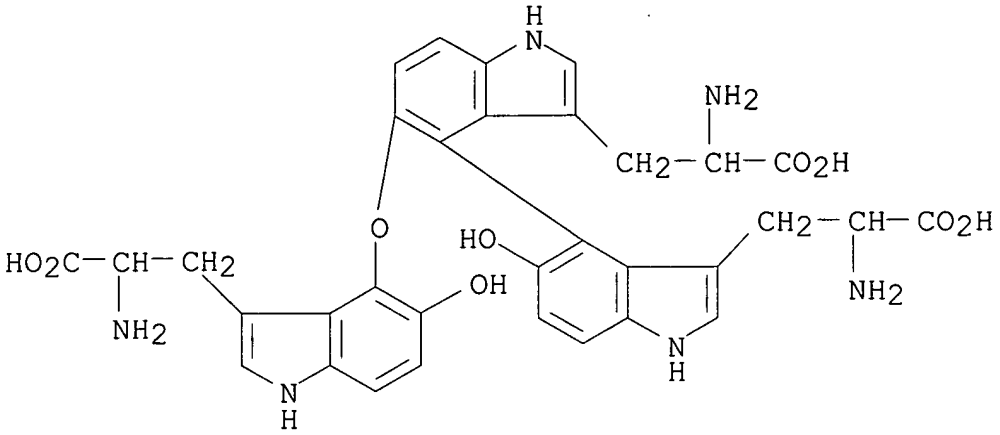
CN [4,4':6',4''-Ter-1H-indole]-3,3',3''-tripropanoic acid, .alpha.,.alpha.',.alpha.''-triamino-5,5',5''-trihydroxy-, [.alpha.S-(.alpha.R*,.alpha.'R*,.alpha.''R*)]- (9CI) (CA INDEX NAME)



RN 147502-87-2 ZCA
CN [4,6'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-4'-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-5,5'-dihydroxy-, [.alpha.S-[.alpha.R*,.alpha.'R*,4'(R*)]]- (9CI) (CA INDEX NAME)

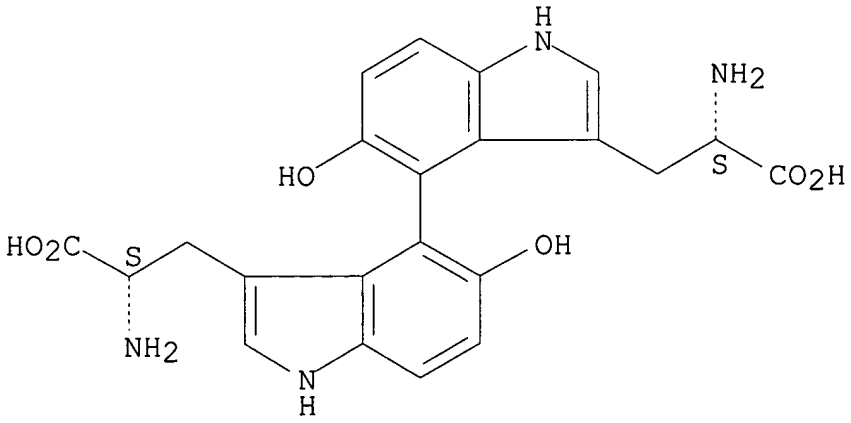


RN 147502-89-4 ZCA
CN [4,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-5-[[3-(2-amino-2-carboxyethyl)-5-hydroxy-1H-indol-4-yl]oxy]-5'-hydroxy-, [.alpha.S-[.alpha.R*,.alpha.'R*,5(R*)]]- (9CI) (CA INDEX NAME)



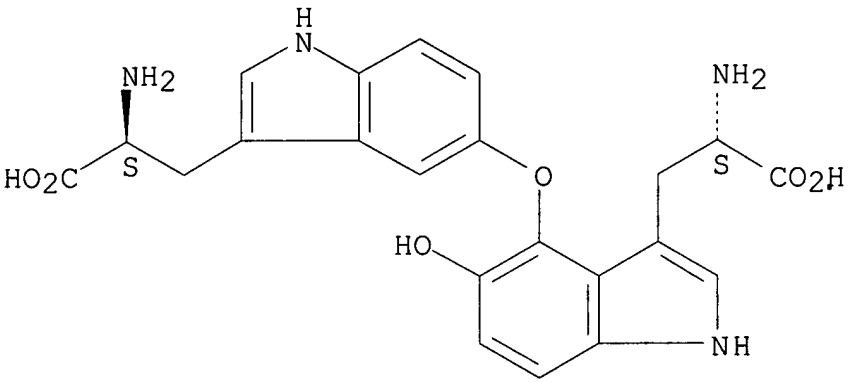
IT **129784-89-0P 147502-85-0P**
(formation of, in electrochem. and enzymic oxidn. of hydroxytryptophan)
RN 129784-89-0 ZCA
CN [4,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-5,5'-dihydroxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147502-85-0 ZCA
CN L-Tryptophan, 4-[[3-(2-amino-2-carboxyethyl)-1H-indol-5-yl]oxy]-5-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **129738-78-9 147502-87-2 147502-89-4**
(cyclic voltammetry of, electrochem. and enzymic oxidn. of hydroxytryptophan in relation to)
IT **129784-89-0P 147502-85-0P**
(formation of, in electrochem. and enzymic oxidn. of hydroxytryptophan)

L11 ANSWER 28 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 117:251791 ZCA
TITLE: Preparation of 5-oxo-1-proline peptides as drugs
INVENTOR(S): Poli, Stefano; Coppi, Germano
PATENT ASSIGNEE(S): Poli Industria Chimica S.p.A., Italy
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 498268	A2	19920812	EP 1992-101347	19920128
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EP 498268	A3	19931208		
R: DE, ES, FR				
PRIORITY APPLN. INFO.:			IT 1991-MI303 A	19910206
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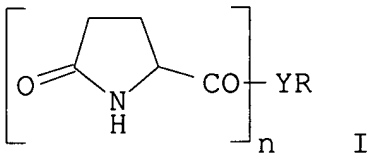
OTHER SOURCE(S): MARPAT 117:251791
GI



I

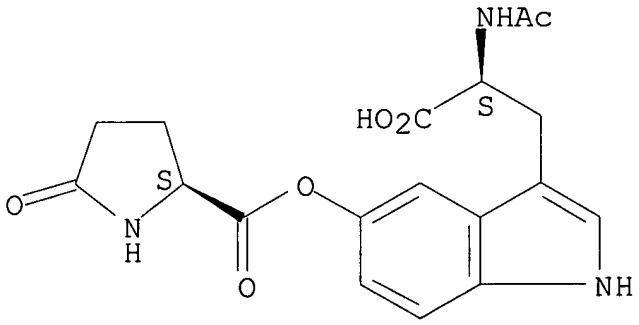
AB Title compds. I (Y = O, S, NH, pyrrolidinyl, thiazolidinyl; R, when Y = O, S, is such that R-YH = C2-5 hydroxy- or thiolalkylamine, C3-11 L-hydroxy or thiolamino acid, which can be aliph, arom., a hydroxy- or thiol-oligopeptide contg. 2-6 amino acid units, or an ester, amide or N-acyl deriv thereof, etc.; n = 1-3, such that when n = >1, R is a residue having .gtoreq.2 YH groups), were prepd. L-5-Hydroxytryptophan Me ester and 5-oxoproline in DMF were stirred with DCC to give N-(5-oxo-L-prolyl)-L-5-hydroxytryptophan. I showed immunostimulatory, antiradical, and superoxide stimulating activities comparable to or greater than those of pyroglutamylthiazolidinecarboxylic acid.

IT **144379-61-3P 144379-78-2P**
(prepn. of, as drug)

RN 144379-61-3 ZCA

CN L-Tryptophan, N-acetyl-5-hydroxy-, ester with 5-oxo-L-proline (9CI) (CA INDEX NAME)

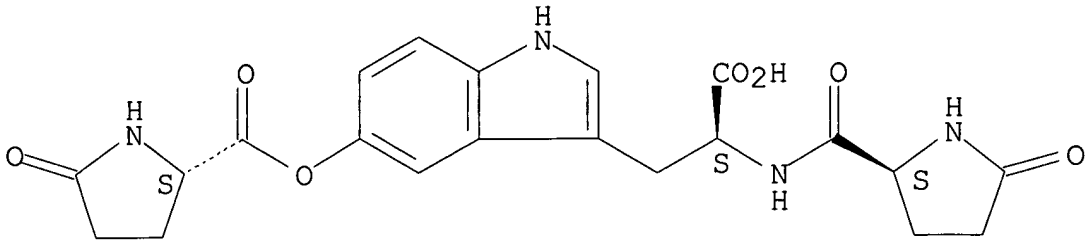
Absolute stereochemistry.



RN 144379-78-2 ZCA

CN L-Tryptophan, 5-hydroxy-N-(5-oxo-L-prolyl)-, ester with 5-oxo-L-proline (9CI) (CA INDEX NAME)

Absolute stereochemistry.



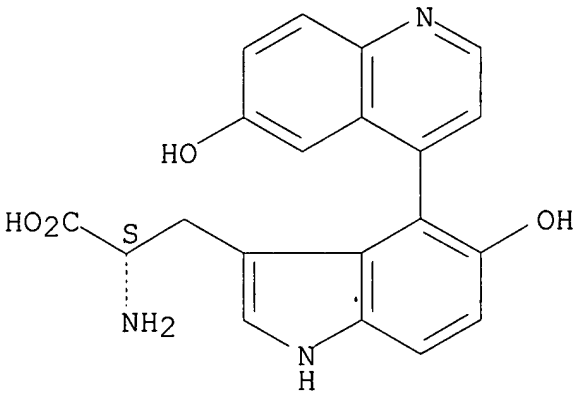
IT **144379-61-3P 144379-78-2P**
(prepn. of, as drug)

L11 ANSWER 29 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 113:161033 ZCA
TITLE: Biomimetic electrochemistry. A study of the electrochemical and peroxidase-mediated oxidation of 5-hydroxytryptophan
AUTHOR(S): Humphries, Keith; Dryhurst, Glenn
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. Oklahoma, Norman, OK, 73019, USA
SOURCE: Journal of the Electrochemical Society (**1990**), 137(4), 1144-9
CODEN: JESOAN; ISSN: 0013-4651
DOCUMENT TYPE: Journal
LANGUAGE: English

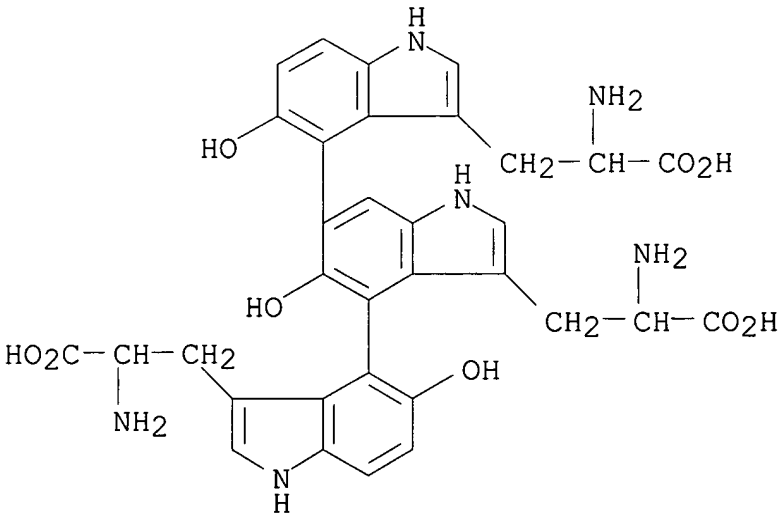
AB The electrochem.-driven and peroxidase-mediated oxidns. of 5-hydroxytrpytophan (5-HTPP) in acidic soln. have been studied. Both oxidn. processes yield a complex mixt. of identical products. Under a limited set of exptl. conditions, the first voltammetric oxidn. peak of 5-HTPP at a pyrolytic graphite electrode exhibits linear diffusion control. Based upon the peak characteristics it may be implied that the initial step in the electrooxidn. is a reversible one-electron abstraction to give a radical cation that deprotonates to a neutral radical, 5-HTPP.bul.. Attack by 5-HTPP on this radical leads to three sets of diastereomeric dimers. 5-HTPP.bul. can also be further oxidized (1e-) to a quinone imine that is attacked by water and then oxidized to give tryptophan-4,5-dione. Addnl. chem./electrochem. reactions generate other products including one fully characterized trimer. The electrochem. process appears to exactly mimic the enzymic reaction.

IT **129715-18-0P 129738-78-9P 129784-89-0P**
(formation of, in electrochem. and peroxidase-mediated oxidn. of hydroxytyptophan in acid soln.)
RN 129715-18-0 ZCA
CN L-Tryptophan, 5-hydroxy-4-(6-hydroxy-4-quinolinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

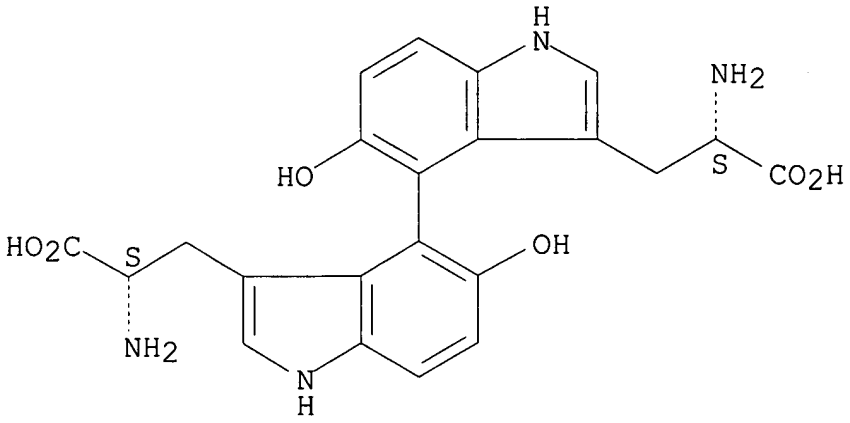


RN 129738-78-9 ZCA
CN [4,4':6',4''-Ter-1H-indole]-3,3',3''-tripropanoic acid, .alpha.,.alpha.',.alpha.''-triamino-5,5',5''-trihydroxy-, [.alpha.S-(.alpha.R*,.alpha.'R*,.alpha.''R*)]- (9CI) (CA INDEX NAME)



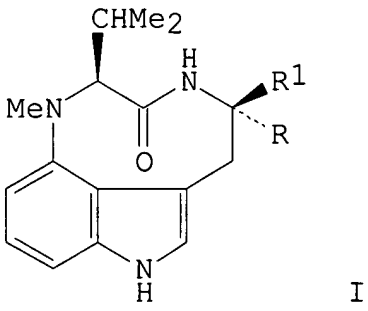
RN 129784-89-0 ZCA
CN [4,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-5,5'-dihydroxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **129715-18-0P 129738-78-9P 129784-89-0P**
(formation of, in electrochem. and peroxidase-mediated oxidn. of hydroxytyptophan in acid soln.)

L11 ANSWER 30 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 112:55378 ZCA
TITLE: Efficient syntheses and chemistry of indolactam-V and its analogs
AUTHOR(S): Masuda, Toshiya; Nakatsuka, Shinichi; Goto, Toshio
CORPORATE SOURCE: Fac. Agric., Nagoya Univ., Nagoya, 464, Japan
SOURCE: Agricultural and Biological Chemistry (**1989**), 53(8), 2257-60
CODEN: ABCHA6; ISSN: 0002-1369
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:55378
GI



I

AB The tumor promoter, indolactam-V (I, R = CH2CH, R1 = H), was prepd.

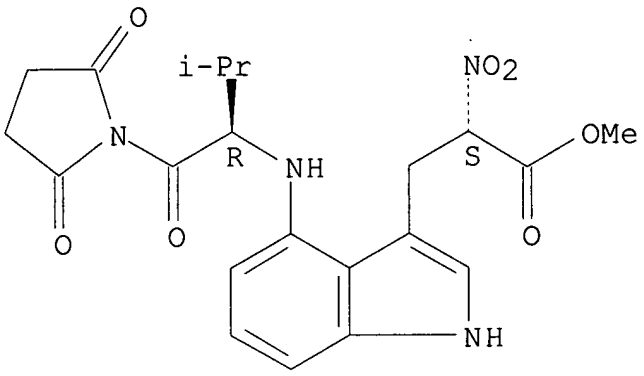
in 8 steps and a 15% overall yield from Me 4-nitroindole-3-carboxylate. Some chem. properties of indolactam-V analogs I (R = CO2Me, R1 = H; R = H, R1 = CO2Me) were investigated.

IT **124549-58-2P 124568-66-7P**
(prepn. and reductive cyclization of)

RN 124549-58-2 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[(2,5-dioxo-1-pyrrolidinyl)carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, methyl ester, (R*,S*)- (9CI) (CA INDEX NAME)

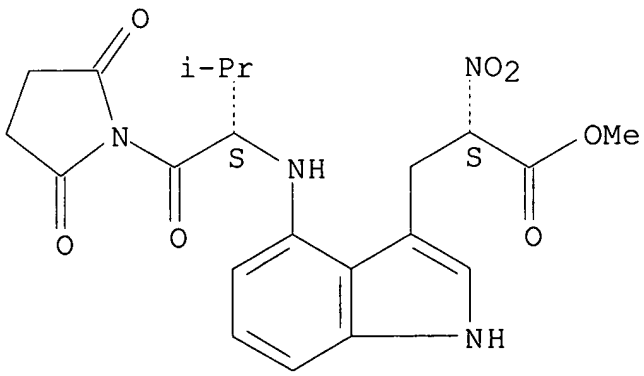
Relative stereochemistry.



RN 124568-66-7 ZCA

CN 1H-Indole-3-propanoic acid, 4-[[1-[(2,5-dioxo-1-pyrrolidinyl)carbonyl]-2-methylpropyl]amino]-.alpha.-nitro-, methyl ester, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **124549-58-2P 124568-66-7P**
(prepn. and reductive cyclization of)

L11 ANSWER 31 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 112:7383 ZCA
TITLE: Preparation of dihydropyridine-containing prodrugs for brain-specific drug delivery
INVENTOR(S): Bodor, Nicholas S.
PATENT ASSIGNEE(S): University of Florida, USA
SOURCE: U.S., 282 pp. Cont.-in-part of U.S. 4,479,932.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4824850	A	19890425	US 1984-665940	19841029
US 4479932	A	19841030	US 1982-379316 <--	19820518
US 4622218	A	19861111	US 1983-475493 <--	19830315
EP 218300	A2	19870415	EP 1986-201710 <--	19830512
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EP 224283	A2	19870603	EP 1986-201713	19830305

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EP 224283 A3 19880921
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US 5187158	A	19930216	US 1991-639283 <--	199101 10
US 5525727	A	19960611	US 1992-967979 <--	199210 28
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			US 1983-475493 <--	A2 198303 15
			CA 1983-428192 <--	A 198305 16
			US 1983-516382 <--	A2 198307 22
			JP 1982-101940 <--	A 198206 14
			EP 1983-902034 <--	P 198305 12
			WO 1983-US725	A 198305

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	ZA 1983-3521	A	198305 17
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OTHER SOURCE(S): CASREACT 112:7383; MARPAT 112:7383
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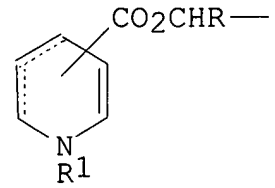
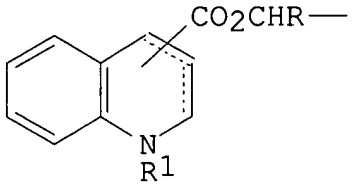
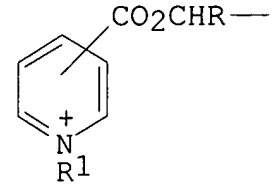
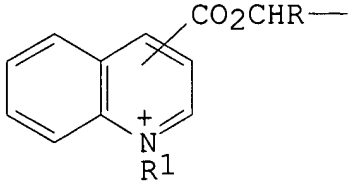
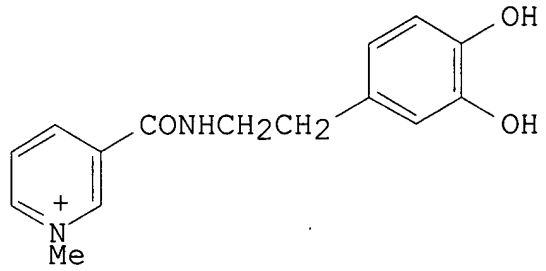
Q1= 

Q2= 

Q3= 

Q4= 



III

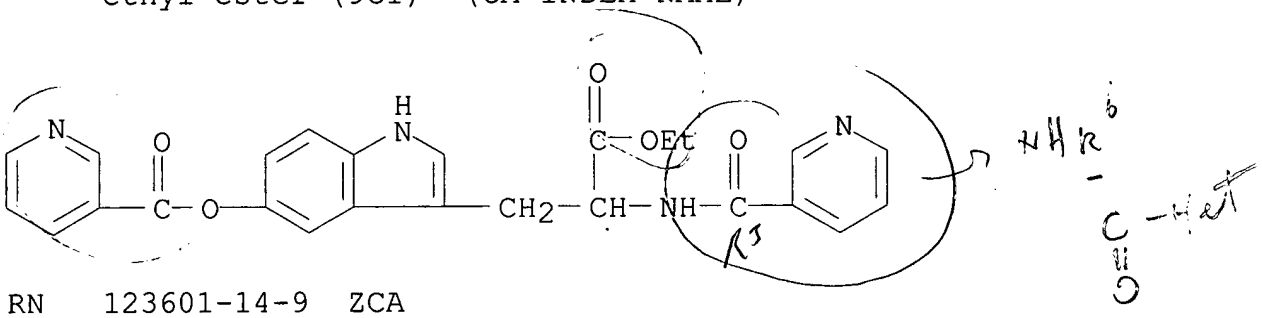
AB Compds. of the formula D(DHC)n (I) [D = residue of a centrally acting drug having anticonvulsant, sedative and/or hypnotic properties, said drug being a hydantoin or barbiturate or an analog of a hydantoin or barbiturate, said drug contg. at least one reactive amide or imide functional group, said residue being characterized by the absence of a H atom from at least one of said amide or imide functional groups in said drug; n = pos. integer equal to the no. of said functional groups from which a H atom is absent; DHC = reduced, biooxidizable, blood-brain barrier penetrating, lipoidal form of a dihydropyridine-pyridinium salt redox carrier; DHC = Q1, Q2, etc.; R = H, C1-7 alkyl, C3-8 cycloalkyl, C1-7 haloalkyl, etc.; R1 = C1-7 alkyl, haloalkyl, C7-10 aralkyl; dotted line indicates the presence of a double bond in position 4 or 5 of the dihydropyridine ring or position 2 or 3 of the dihydroquinoline ring] were prepd. as brain-specific prodrugs. Quaternary salts of the formula D(QC+)nqX-t (II) (D = as given above; X- = anion of a pharmaceutically acceptable org. or inorg. acid; t = valence of acid anion; q = no. which when multiplied by t is equal to n; QC+ = hydrophilic, ionic pyridinium salt form of a dihydropyridine-pyridinium salt redox carrier; QC+ = Q3, Q4, etc.;

R, R1 = as given above; n = pos. integer equal to the no. of said functional groups from which a H atom is absent) were prepd. as intermediates for I. Reaction of 5,5-diphenyl-3-hydroxymethyl-2,4-imidazolidinedione with nicotinic anhydride, followed by methylation with MeI and redn., gave 5,5-diphenyl-3-[(1'-methyl-1',4'-dihydropyridin-3'-yl)carbonyloxymethyl]-2,4-imidazolidinedione. After one single injection of 1-methyl-3-[[N-[.beta.-(3,4-dipivalyloxyphenyl)ethyl]]carbamoyl-1,4-dihydropyridine to a rat, the pyridinium compd. III could be seen to appear and then to disappear quickly from the blood, with a half-life of 27 min. On the contrary, the concn. of III increases in the brain steadily, reaching a max. at about 30 min following administration. For III, the half-life of diappearance from the brain is about 3.2 h.

IT **123601-13-8P 123601-14-9P**
(prepn. and reaction of, in prepn. of brain-specific prodrug)

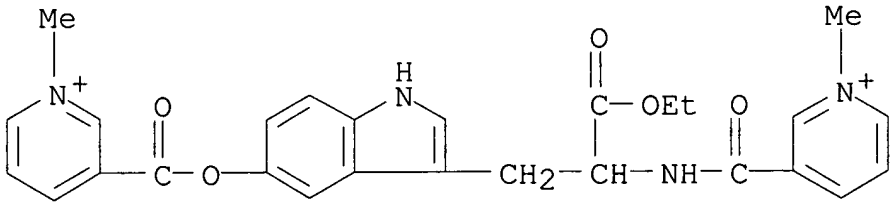
RN 123601-13-8 ZCA

CN Tryptophan, N-(3-pyridinylcarbonyl)-5-[(3-pyridinylcarbonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 123601-14-9 ZCA

CN Pyridinium, 3-[[[3-[3-ethoxy-2-[[(1-methylpyridinium-3-yl)carbonyl]amino]-3-oxopropyl]-1H-indol-5-yl]oxy]carbonyl]-1-methyl-, diiodide (9CI) (CA INDEX NAME)



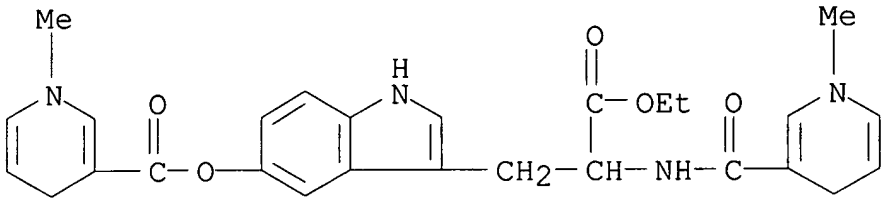
●2 I^-

IT **123600-91-9P**
(prepn. of, as brain-specific prodrug)

RN 123600-91-9 ZCA

CN Tryptophan, N-[(1,4-dihydro-1-methyl-3-pyridinyl)carbonyl]-5-[[(1,4-

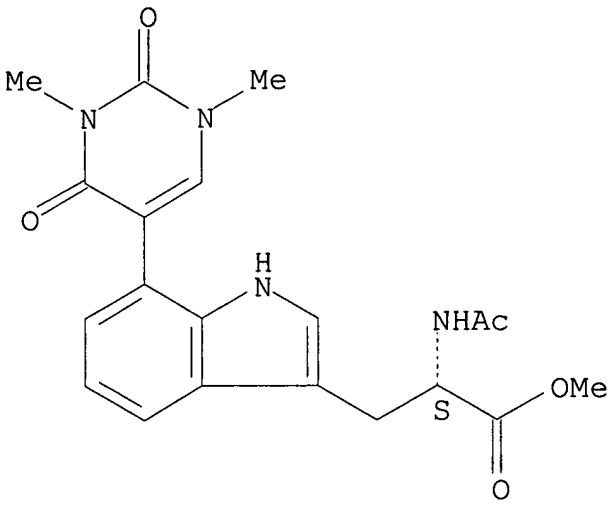
dihydro-1-methyl-3-pyridinyl)carbonyl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



IT **123601-13-8P 123601-14-9P**
(prepn. and reaction of, in prepn. of brain-specific prodrug)
IT **123600-91-9P**
(prepn. of, as brain-specific prodrug)

L11 ANSWER 32 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 111:228035 ZCA
TITLE: Photochemical coupling of 5-bromo-1,3-dimethyluracil and its 6-alkyl derivatives to 3-methylindole and N.alpha.-acetyl-L-tryptophan methyl ester
AUTHOR(S): Celewicz, Lech
CORPORATE SOURCE: Fac. Chem., Adam Mickiewicz Univ., Poznan, 60-780, Pol.
SOURCE: Journal of Photochemistry and Photobiology, B: Biology (**1989**), 3(4), 565-74
CODEN: JPPBEG; ISSN: 1011-1344
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:228035
AB Photochem. reactions between 5-bromo-1,3-dimethyluracils and 3-substituted indoles in acetone soln. were studied. Irradn. (.lambda. > 290 nm) of 5-bromo-1,3-dimethyluracil and N.alpha.-acetyl-L-tryptophan Me ester (I) yields, in addn. to 5-(2-indolyl)uracil, a new photoadduct, 5-(7-indolyl)uracil. 5-Bromo-1,3-dimethyluracils with 6-alkyl substituents irradiated in the presence of I give the 5-(2-indolyl)uracil-type photoadducts exclusively.
IT **123739-87-7P**
(prepn. of, photochem.)
RN 123739-87-7 ZCA
CN L-Tryptophan, N-acetyl-7-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-5-pyrimidinyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



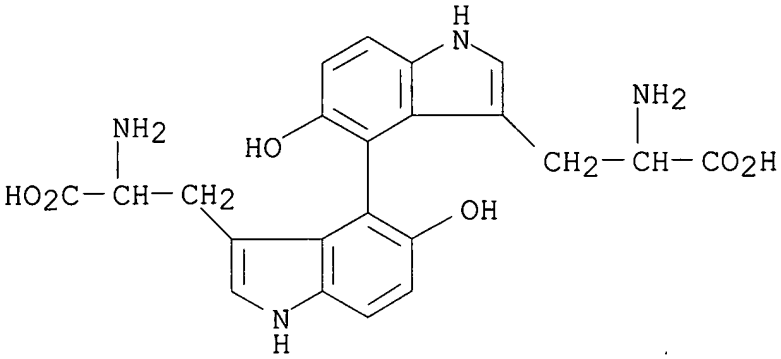
IT **123739-87-7P**
(prepn. of, photochem.)

L11 ANSWER 33 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 108:37484 ZCA
TITLE: Electrochemical oxidation of 5-hydroxytryptophan in acid solution
AUTHOR(S): Humphries, Keith; Dryhurst, Glenn
CORPORATE SOURCE: Dep. Chem., Univ. Oklahoma, Norman, OK, 73019, USA
SOURCE: Journal of Pharmaceutical Sciences (**1987**), 76(10), 839-47
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

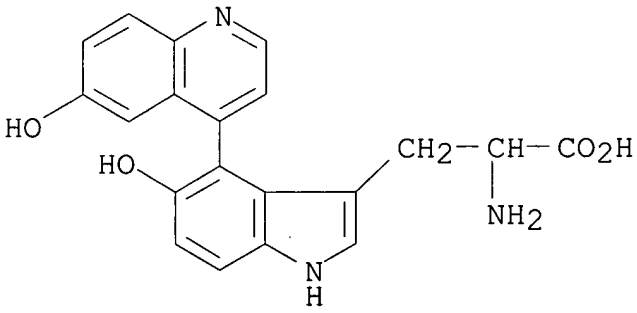
AB The electrochem. oxidn. of 5-HTP (I) in acid soln. proceeds by an initial 1e-, 1H+ reaction to a radical intermediate. This radical can dimerize and 3 diastereomers of 4,4'-bis(5-hydroxytryptophan) have been isolated and characterized. The radical can also undergo further electrochem. oxidn. (1e-, 1H+) to a quinoneimine intermediate. Nucleophilic attack by water on this quinoneimine, followed by further oxidn., gives tryptophan-4,5-dione. Nucleophilic attack by I on the quinoneimine gives a dimeric indolenine which undergoes a complex series of chem. and electrochem. reactions leading ultimately to 4-[1-(6-hydroxyquinolyl)]-5-hydroxytryptophan. Two diastereomers of the latter compd. have been isolated and characterized.

IT **112241-67-5P 112241-69-7P**
(formation of, in hydroxytryptophan electrochem. oxidn.)
RN 112241-67-5 ZCA

CN [4,4'-Bi-1H-indole]-3,3'-dipropanoic acid, .alpha.,.alpha.'-diamino-5,5'-dihydroxy- (9CI) (CA INDEX NAME)



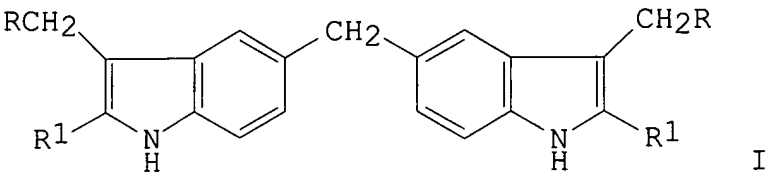
RN 112241-69-7 ZCA
CN Tryptophan, 5-hydroxy-4-(6-hydroxy-4-quinolinyl)- (9CI) (CA INDEX NAME)



IT **112241-67-5P 112241-69-7P**
(formation of, in hydroxytryptophan electrochem. oxidn.)

L11 ANSWER 34 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 99:87984 ZCA
TITLE: Some alkylation reactions of bis[(dimethylamino)methyl] derivatives of di-5-indolylmethane
AUTHOR(S): Samsoniya, Sh. A.; Chikvaidze, I. Sh.; Suvorov, N. N.
CORPORATE SOURCE: Tbilis. Gos. Univ., Tbilisi, USSR
SOURCE: Soobshcheniya Akademii Nauk Gruzinskoi SSR (**1983**), 109(1), 73-6
CODEN: SAKNAH; ISSN: 0002-3167
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 99:87984

GI



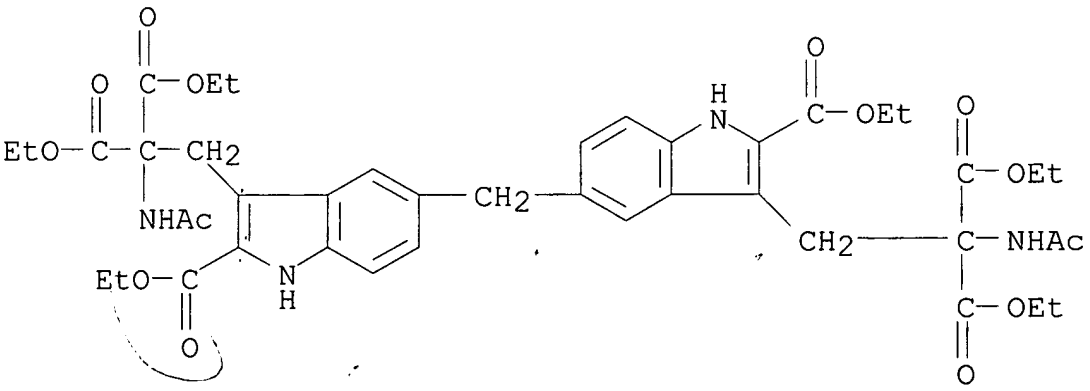
I

AB Quaternization of I (R = Me2N, R1 = H, CO2Et) (II) with Me2SO4 gave the methosulfates, which with KCN gave I (R = CN). II and AcNHCH(CO2Et)2 gave I [R = (EtO2C)2C(NHAc); R1 = H, CO2Et].

IT **86815-82-9P 86815-83-0P**
(prepn. of)

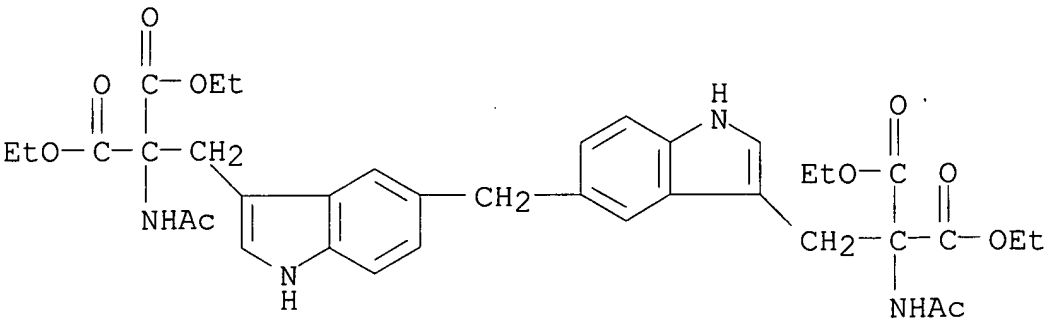
RN 86815-82-9 ZCA

CN Propanedioic acid, 2,2'-[methylenebis[[2-(ethoxycarbonyl)-1H-indole-5,3-diyl]methylene]]bis[2-(acetylamino)-, tetraethyl ester (9CI) (CA INDEX NAME)



RN 86815-83-0 ZCA

CN Propanedioic acid, 2,2'-[methylenebis(1H-indole-5,3-diylmethylene)]bis[2-(acetylamino)-, tetraethyl ester (9CI) (CA INDEX NAME)



IT **86815-82-9P 86815-83-0P**
(prepn. of)

L11 ANSWER 35 OF 35 ZCA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 68:49447 ZCA
TITLE: Derivatives of .alpha.-aminoindole-3-acetic and -propionic acids
INVENTOR(S): Shen, Tsung-Ying
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3316260		19670425	US 1965-505036	19651024

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GI For diagram(s), see printed CA Issue.

AB The title compds. (I) were prepd. via II. I had pyretic and a high degree of antiinflammatory activity useful in the treatment of arthritic and dermatological disorders. Thus, to a stirred soln. of 0.005 mole oxalyl chloride in 15 ml. anhyd. Et2O was added 0.005 mole 2-methyl-5-methoxyindole in 15 ml. Et2O over about 30 min., the mixt. stirred under N several hrs., concd. to one half its vol., 4 ml. tert-BuOH added, the mixt. stirred several hrs., excess tert-BuOH and Et2O removed, and the residue chromatographed on a silica gel column to give II(A = H, R2 = Me, R = COCO2Bu-tert, R5 = OMe). A soln. of 40 g. levulinic acid in 300 ml. hot H2O was added to 65 g. p-methoxyphenylhydrazine hydrochloride in 700 ml. hot H2O

with stirring, and the mixt. stirred 0.5 hr. to give the hydrazone (III). A mixt. of 42 g. III, 120 g. ZnCl2, and 100 ml. abs. EtOH was refluxed 18 hrs., cooled, and poured into dil. HCl with stirring, the ppt. sepd. and taken up in EtOH, the soln. evapd. in vacuo, the syrup dissolved in Et2O, the ether extd. with 10% Na2CO3, and the aq. soln. acidified to give II(A = H, R5 = OMe, R = CH2CO2H, R2 = Me). A mixt. of 0.1 mole II(A = H, R5 = OMe, R = CH2CO2H, R2 = Me), 300 ml. abs. EtOH, and 10 ml. concd. H2SO4 was refluxed 6 hrs. under N and the mixt. worked up to give II(A = H, R5 = OMe, R2 = Me, R = CH2CO2Et). A mixt. of 2-methyl-4-trifluoromethylindole3-acetic acid and 2-methyl-6-trifluoromethylin-dole-3-acetic acid was similarly prepd. and sepd. by chromatog. A soln. of 0.15 mole p-fluorophenylhydrazine hydrochloride and 0.12 mole Et levulinate in 250 ml. 2N ethanolic HCl was heated on a steam bath a few min., until an exothermic reaction took place, then refluxed 30 min. to give on work up II(A = H, R5 = F, R = CH2CO2Et, R2 = Me). Under N a mixt. of 150 ml. abs. EtOH, 0.145 mole anhyd. AcONa, and 0.125 mole p-methoxyphenylhydrazine hydrochloride was held at 20-5.degree. 30 min., 0.142 mole benzoyl-propionic acid added all at once, the mixt. kept at room temp. 30 min., 18 g. anhyd. HCl in EtOH added over 20 min., and the mixt. heated on a steam bath 2 hrs. and worked up to give II(R = CH2CO2Et, R2 = Ph, R5 = OMe, A = H). II(R = CH2CO2Et, R2 = H, R5 = OMe, A = H) (1 mole) was gradually added to a soln. obtained from 1 mole Na, 5 moles EtOH, and 1 mole Et oxalate, the mixt. kept at room temp. 5 hrs., the solvent removed in vacuo, the residue dissolved in 1.2 l. H2O, the pH adjusted to 2 with HCl, and the mixt. extd. with Et2O to give II(R = CH2CO2Et, R2 = COCO2Et, R5 = OMe, A = H) (IV). IV boiled 5 hrs. in 6 moles AcOH contg. 2 g. p-toluenesulfonic acid with the formed EtOAc distd. and the mixt. worked up to give II(R5 = OMe, R2 = H, R = CH2COCO2H, A = H). A mixt. of 0.05 mole N,N-dicyclohexylcarbodiimide in a min. vol. of tetrahydrofuran (THF) and 0.1 mole II(R = CH2COCO2H, R5 = OMe, R2 = Me, A = H) was kept overnight at room temp. and filtered and the solvent removed in vacuo to give the corresponding anhydride. A mixt. of 100 ml. tert-BuOH, 0.3 g. fused ZnCl2, and the prepd. anhydride was refluxed under N overnight and filtered, the solvent removed in vacuo, 500 ml. CHCl3 added, and the CHCl3 soln. worked up to give II(R5 = OMe, R2 = Me, R = CH2COCO2Bu-tert, A = H). II(R5 = OMe, R2 = Me, R = CH2COCO2Bu-tert, A = H) was treated with an ether soln. of diazomethane to give the Me ester. A mixt. of 0.1 mole sodium benzylate in 1 l. dioxane under N was gradually added with stirring to 1.2-1.5 l. dioxane at 0-5.degree. contg. 0.1 mole II(R5 = OMe, R2 = Me, R = CH2COCO2H, A = H) anhydride and the mixt. stirred at 20-5.degree. 2 hrs. and acidified with HCl to pH 3 to give II(R5 = OMe, R2 = Me, R = CH2COCO2CH2Ph, A = H). A mixt. of 0.01 mole II(R5 = NO2, R2 = Me, R = CH2COCO2Bu-tert, A = H), 150 ml. tert-BuOH, 15 ml. glacial AcOH, 5 ml. 37% aq. HCHO, and 4 g. Raney Ni was treated with H at 40 psi., the mixt. filtered and concd. in

vacuo to about 25 ml., 250 ml. Et2O added, washed, and the mixt. worked up to give II(R5 = NEt2, R2 = Me, R = CH2COCO2Bu-tert, A = H). II(R5 = NO2, R2 = Me, R = CH2COCO2Bu-tert, A = H) in tert-BuOH was hydrogenated at 25.degree./1 atm. over 10% Pd-C to give II(R5 = NH2, R2 = Me, R = CH2COCO2Bu-tert, A = H). A mixt. of 0.01 mole II(R5 = OMe, R2 = Me, R = CH2COCO2Bu-tert, A = H), 0.02 mole benzyloxyamine, 5 ml. pyridine, and 20 ml. tert-BuOH was heated on the steam bath under N 3 hrs., concd. in vacuo to about 10 ml., and poured into 250 ml. of an ice-H2O mixt. and the org. material collected, washed with H2O and dried to give I(R5 = OMe, n = 1, R1R2 = NOCH2Ph, M = OBu-tert, A = HO). A soln. of 0.021 mole II(R5 = OMe, R2 = Me, R = COCO2Bu-tert, A = H) in 20 ml. HCONMe2 (DMF) was added dropwise to a cold suspension of 1.0 g. NaH (52% dispersion in mineral oil) and 25 ml. DMF, stirred at room temp. 20 min., cooled, treated with 0.0222 mole p-chlorobenzoyl chloride, stirred at room temp. 16 hrs., poured into 260 ml. ice H2O, and extd. with ether and the ether ext. worked up to give II(R5 = OMe, R2 = Me, R = COCO2Bu-tert, A = COC6H4Cl-p). A mixt. of 1.5 g. I(R5 = NH2, R1R2 = NOCH2Ph, n = 1, A = COC6H4Cl-p, M = OBu-tert). 1,4-Dibromobutane (1 g.), 0.975 g. anhyd. Na2CO3, and 80 ml. EtOH was refluxed under N 6 hrs., filtered, the filtrate concd. in vacuo, dild. with Et2O, washed with H2O, dried, and concd. in vacuo to give I(R5 = 1-pyrrolidinyl, R1R2 = NOCH2Ph, n = 1, M = OBu-tert). A mixt. of 0.02 mole I(R5 = NH2, R1R2 = NOCH2Ph, n = 1, M = OBu-tert, A = COC6H4Cl-p), 0.44 mole ethylene oxide, 0.03 mole AcOH, and 300 ml. dimethoxyethane was heated to 100.degree. 18 hrs. in an autoclave, dild. with H2O, and filtered to give I (R5 = N(CH2CH2OH)2, R1R2 = NOCH2Ph, n = 1, A = COC6H4Cl-p). The prepd. material was stirred with a 2 molar proportion of p-toluenesulfonyl chloride in pyridine and poured into H2O, the 5-bis(p-tolylsulfonyloxyethyl)amino compd. isolated and dissolved in C6H6, 1 mole methylamine added, and the mixt. kept at room temp. 3 days, poured into iced-H2O contg. 2 equivs. Na2CO3, and extd. with Et2O immediately to give I(R5 = 4-methyl-1-piperazinyl, R1R2 = NOCH2Ph, M = OBu-tert, n = 1, A = COC6H4Cl-p). A soln. of 0.1 mole tosyl chloride in 200 ml. C6H6 was added dropwise with stirring to a soln. of I(R5 = N(CH2CH2OH)2, R1R2 = NOCH2Ph, M = OBu-tert, n = 1, A = COC6H4Cl-p) and 0.3 mole pyridine in 300 ml. C6H6 at room temp. and the mixt. refluxed 3 hrs., washed with H2O, dried, and evapd. to give I(R5 = morpholino, R1R2 = NOCH2Ph, M = OBu-tert, n = 1, A = COC6H4Cl-p). A mixt. of 0.01 mole II(R5 = OMe, R2 = Me, R = COCO2Bu-tert, A = COC6H4Cl-p), 0.02 mole NH2OH.HCl, 20 ml. tert-BuOH, and 5 ml. pyridine was heated on the steam bath under N 3 hrs., concd. in vacuo, and poured into about 250 ml. ice-H2O mixt., the org. matter collected, washed with H2O until the pyridine odor was removed, dried, dissolved in 25 ml. EtOH and 0.02 mole 38% HCl, and reduced with H at 3000 psi. at room temp. over 1 g. 5% Pd-C, the mixt. filtered, 50 ml. 2.5N HCl added, and the soln. worked up and chromatographed to give I(R5= OMe, R1 =

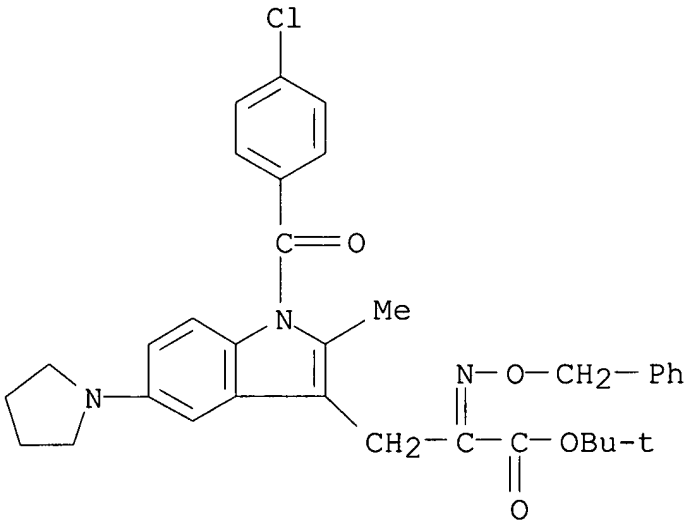
NH2, R2 = H, n = 0, M = OBu-tert, A = COC6H4Cl-p). A mixt. of 0.01 mole I(R5 = OMe, R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 0, M = OBu-tert), 0.011 mole MeI, and 0.015 mole NaHCO3 in 50 ml. anhyd. 1,2-dimethoxyethane was heated on the steam bath under N 3 hrs. and filtered, the solvent removed in vacuo, and the residue chromatographed to give the corresponding .alpha.-methylamino acetate. The .alpha.-dimethylamino acetate was similarly prepd. Also prepd. were: I(R5 = R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 0, M = OBu-tert); I(R5 = OMe, R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 1, M = OBu-tert); I(R5 = R1 = NMe2, R2 = H, n = 0, M = OBu-tert, A = COC6H4Cl-p); I(R5 = R1 = NH2, R2 = H, n = 0, M = OBu-tert); II(R5 = OMe, R = H, R2 = Me, A = COC6H4Cl-p); I(R5 = OMe, R1 = NMe2, R2 = H, n = 0, A = COC6H4Cl-p, M = OEt); I(R5 = OMe, R1R2 = NOCH2Ph, A = H, n = 0, M = OBu-tert); p-nitrophenyl nicotinate; I(R5 = OMe, R1R2 = NOCH2Ph, A = nicotinoyl, n = 0, M = OBu-tert); I(R5 = OMe, R1 = NH2, R2 = H, A = nicotinoyl, n = 0, M = OBu-tert); I(R5 = OMe, R1 = morpholino, R2 = H, A = H, n = 0, M = OEt); I(R5 = OMe, R1 = morpholino, R2 = H, A = COC6H4Cl-p, n = 0, M = OEt); I(R5 = OMe, R1 = NHMe, R2 = H, A = COC6H4Cl-p, n = 0, M = OEt); 2-methyl-5-methoxygramine; I(R5 = OMe, R1 = NO2, R2 = Me, A = H, n = 1, M = OEt); I(R5 = OMe, R1 = Me, R2 = NO2, A = H, n = 1, M = OH); II(R5 = OMe, R = CH2NHCH2CO2H, R2 = Me, A = COCH2C6H4Cl-p). I(R5 = OMe, R1 = NH2, R2 = H, A = COCH2C6H4Cl-p, n = 0, M = OH) (0.001 mole) and 0.001 mole NaOH in 100 ml. H2O was stirred until soln. was complete and filtered and the H2O removed in vacuo to give the corresponding Na salt. The morpholine salt was also prepd. A mixt. of 0.049 mole dicyclohexylcarbodiimide, 0.1 mole I(R5 = OMe, R1 = NMe2, R2 = H, A = COCH2C6H4Cl-p, n = 0, M = OH), and 200 ml. THF was kept at room temp. 2 hrs. and filtered and the filtrate evapd. in vacuo to give the corresponding anhydride. Also prepd. were: anhydrides of I(R5 = OMe, R1 = NHMe, R2 = H, A = COC6H4Cl-p, n = 0, M = OH) and I(R5 = OMe, R1 = NHBu-iso, R2 = H, A = COC6H4Cl-p, n = 0, M = OH). Also prepd. were: I(R5 = OH, R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 0, M = OH); I(R5 = OMe, R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 0, M = NMe2); II(R5 = OMe, R2 = Me, R = COCO2H, A = COC6H4Cl-p); I(R5 = OH, R1 = NH2, R2 = H, A = COC6H4OMe-p, n = 0, M = OBu-tert); I(R5 = OH, R1 = NH2, R2 = H, A = COC6H4Cl-p, n = 0, M = OBu-tert); I(R5 = OMe, R1 = morpholino, R2 = H, A = COC6H4CF3-p, n = 0, M = OEt); I(R5 = OMe, R1 = pyrrolidino, R2 = H, A COC6H4Cl-p, n = 0, M = OH); I(R5 = F, R1 = cyclohexylamino, R2 = H, A = COC6H4Me-p, n = 0, M = OH; II(R5 = NH2, R2 = Me, R = COCO2Bu-tert, A = COC6H4Cl-p); II(R5 = NHMe, R2 = Me, R = COCO2Bu-tert, A = COC6H4Cl-p); II(R5 = NO2, R2 = Me, R = COCO2Bu-tert, A = COC6H4Cl-p).

IT **17535-55-6P 17535-57-8P 17845-22-6P**
(prepn. of)

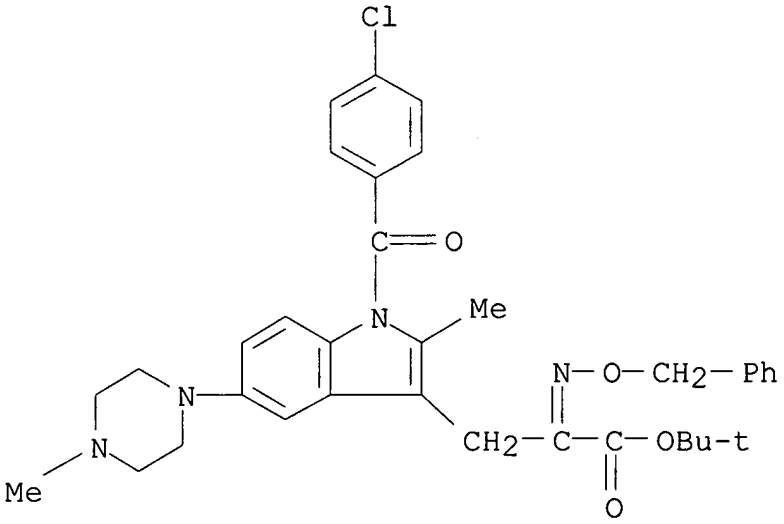
RN 17535-55-6 ZCA

CN Indole-2-pyruvic acid, 1-(p-chlorobenzoyl)-2-methyl-5-(1-

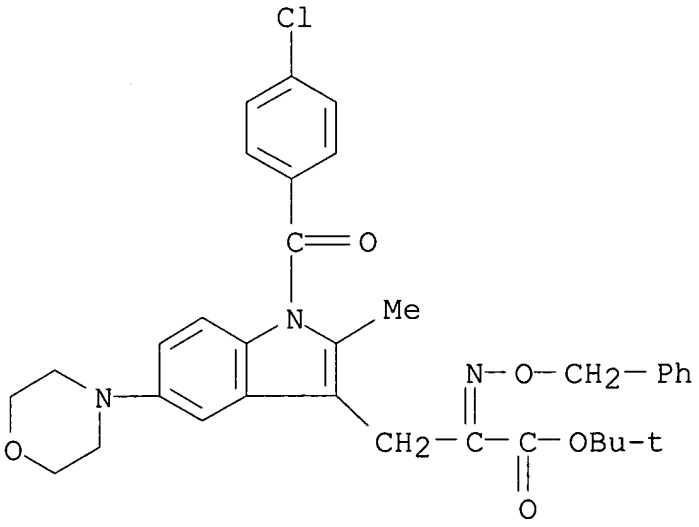
pyrrolidinyl)-, tert-butyl ester, .alpha.-(O-benzyloxime) (8CI) (CA INDEX NAME)



RN 17535-57-8 ZCA
CN Indole-2-pyruvic acid, 1-(p-chlorobenzoyl)-2-methyl-5-(4-methyl-1-piperazinyl)-, tert-butyl ester, .alpha.-(O-benzyloxime) (8CI) (CA INDEX NAME)



RN 17845-22-6 ZCA
CN Indole-2-pyruvic acid, 1-(p-chlorobenzoyl)-2-methyl-5-morpholino-, tert-butyl ester, .alpha.-(O-benzyloxime) (8CI) (CA INDEX NAME)



IT **17535-55-6P 17535-57-8P 17845-22-6P**
(prepn. of)